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THE INCIDENCE AND EFFECTS OF RH INCOMPATIBILITY BETWEEN MOTHER AND CHILD.[1]

By LUCY M. BRYCE, RACHEL JAKOBOWICZ, J. J. GRAYDON AND KATE CAMPBELL.

From the Queen Victoria Hospital, the Red Cross Blood Transfusion Service and the Commonwealth Serum Laboratories, Melbourne.

BLOOD GROUP TESTS, including investigation of the Rh status of mother and child, have formed part of the routine care of patients admitted to the obstetric unit of the Queen Victoria Hospital since 1942; however, the series analysed in this paper is restricted to the years 1946 to 1949 inclusive, since prior to this period the Coombs test and the more modern methods of employing colloid cell suspending media for the detection of antibodies had not been applied.

The series analysed consists of 9533 cases, comprising all deliveries which occurred after the twenty-eighth week of pregnancy, and one case in which the mother and baby were admitted to hospital for investigation on the third day after delivery because of the early onset of severe jaundice in the baby. With the exception of this case, and of one other in which the woman was referred to the hospital for the management of her pregnancy because her previous history strongly suggested Rh incompatibility, there was no selection of cases, apart from the women's own choice of hospital. Pickles (1949*a*) discusses the possible influence of such factors as selective admission to hospital of *primiparæ*, or of *multiparæ* with histories of previous obstetric difficulties, which would respectively tend to reduce or to increase the apparent incidence of *erythroblastosis fœtalis*. She states that these factors pertain to some extent in England, whereas in America, where delivery in hospital is the accepted rule, series based on consecutive deliveries probably give a fairly accurate picture of the disease. We believe that the latter concept largely holds true for our series, since in Melbourne also domiciliary midwifery is rarely practised.

In this paper we have (in deference to the common usage, especially among our obstetricians, and to the preference of the clinical member of our team) included all manifestations of disease in the baby resulting from Rh incompatibility with its mother under the name *erythroblastosis fœtalis*, and for its three main manifestations we have used the terms congenital œdema of the fœtus, *icterus gravis*, and anæmia without jaundice respectively. We consider, however, that neither the term *erythroblastosis fœtalis* nor its most frequently used alternative, hæmolytic disease of the newborn, is fully descriptive of all aspects of the underlying pathology of the disease.

Unless otherwise specified, the generally familiar term Rh-positive has been used to indicate known presence of D (Rh_0) antigen in the cells tested, irrespective of knowledge of presence or absence of the C and E antigens. When relevant, we have alternatively used the more precise term D-positive.

Rh-negative is used to indicate the known absence of C, D and E; D-negative signifies the absence of the D antigen, in the presence of either C (rh') or E (rh").

I. SEROLOGICAL AND STATISTICAL ASPECTS.

(L.M.B., R.J., and J.J.G.)

Scheme of Investigations.

The A B O groups and Rh factors were determined for all women at the time of their first visit to the ante-natal department.

[1] A preliminary review of this material was given at the scientific session of a meetng of the Red Cross National Blood Transfusion Service Committee on February 25, 1950.

For those found to be Rh-negative or D-negative, the serum was examined for Rh antibodies; in cases in which antibodies were found, the serum was reexamined periodically during pregnancy, as far as possible at monthly intervals; for those in whom no Rh antibodies were found at the first examination, the serum was not examined again until the seventh or eighth month of pregnancy.

At or shortly after delivery, blood samples from all women, both Rh-positive and Rh-negative, were examined with a series of cell suspensions, chosen to include among them all three (C, D and E) antigens. The serum of Rh-negative and D-negative mothers was further examined for antibodies during the early puerperium, if their babies' red cells were D-positive or contained the C or E antigens.

The cord blood of all infants, except that of the stillborn who were so macerated that suitable blood samples could not be obtained, was examined for the A B O and Rh factors, and for the reaction to the direct Coombs test. In cases in which the mother's blood contained Rh antibodies, their presence in or absence from the cord blood was also determined.

Technique.

Determination of Rh Factor.

The Rh factor was determined as follows. All cell samples were tested with potent anti-D agglutinating sera by the slide method (Simmons, Graydon, Jakobowicz and Bryce, 1943). Samples found to be D-negative were also tested with anti-C and anti-E agglutinating sera.

Detection of Antibodies.

The serum of Rh-negative and D-negative women was tested with several group O cell samples of suitable Rh types (for example, Rh_1, Rh_2 and Rh-negative) suspended both in saline and in a mixture of four parts of group AB human plasma and one part of 30% bovine albumin (Armour Laboratories). The tests were made on slides incubated in a moist chamber for one hour at 37° C.

In cases in which agglutination occurred with both the saline and the plasma-albumin cell suspensions, or with the latter alone, undiluted serum and dilutions of it in saline (ranging from one in two to one in 2048) were mixed with 5% suspensions of D-positive (group O) cells in saline, and incubated in a moist chamber for two hours at 37° C. If agglutination was detectable by the naked eye or the hand lens, the presence of agglutinating antibodies was recorded, and the reciprocal of the highest dilution in which agglutination was demonstrable was taken as the titre.

To ascertain whether incomplete antibodies were also present to a higher titre than the agglutinating antibodies, the cells in dilutions beyond the agglutinating range were submitted to the indirect Coombs test. In samples in which no agglutination was observed in any serum concentration, the indirect Coombs test was carried out in the whole range, to determine the titre of the incomplete antibodies.

Serum containing anti-D antibodies was further tested by similar technique with cells containing only the C (rh') or E (rh") antigens.

Results and Their Interpretation.

Since our series consists of consecutive cases, it is not unexpected that in a four-year period there were a few instances of more than one delivery of the same woman, but as such repetition is likely to occur in similar proportions of both Rh-positive and Rh-negative women, it does not invalidate the statistical analysis of the series, considered as consecutive deliveries.

As shown in Table I, the incidence (16·7%) of the Rh-negative status in the mothers is within the range to be expected in a population of predominantly Caucasian stock.

Rh antibodies were found in 4·5% of the sera of the Rh-negative women in this series. This figure is close to the usually estimated incidence of under 5% (Pickles, 1949*b*). As would be expected, it was somewhat higher (6·7%) in those whose babies were subsequently found to be Rh-positive. Since even the presence of antibodies in the maternal serum does not necessarily mean that the baby will be affected, it is psychologically important to stress that the babies of at least 95% of all Rh-negative mothers will not be affected by damage due to Rh incompatibility.

Our observation that 60% of the pregnancies of the Rh-negative women in this series resulted in Rh-positive children is close to the expected figure of 58%, calculated from the estimated numbers of matings of these Rh-negative women, approximately 17·5% of whom are likely to be with men who are D-negative, 33·5% with homozygous D-positive men and 49% with heterozygous D-positive men. The majority of women in this series whose serum contained Rh antibodies had Rh-positive children, but in the minority whose babies were Rh-negative there was evidence that the antibodies present were residual from a previous stimulation, either by an earlier pregnancy or by transfusion, presumably with Rh-positive blood.

Type and Specificity of Antibody.

As has been indicated above, we have used the terms "agglutinating" and "incomplete" to describe the two main types of antibodies. The term "incomplete" includes all those detected only by the tests with cells suspended in colloid media.

In this series we did not as a routine measure include the indirect Coombs test in the ante-natal examination for antibodies, but there was no case in which a positive direct Coombs reaction was subsequently obtained with the baby's cells, in which antibodies had not been detected in the maternal serum, at least at delivery, by the methods used.

The incidence and titre range of each type of antibody is shown in Table II. The relationship between antibody titre and clinical findings concerning severity of *erythroblastosis fœtalis* is discussed in the second section of this paper.

In the cord serum, only incomplete antibodies were demonstrable. In Rh-positive babies their titres ranged from traces to 120, as estimated by the indirect Coombs test. In some of these cases, the corresponding maternal serum apparently contained only agglutinating antibodies, but if Wiener's theory (1948) is correct, that only incom-

TABLE I.

Rh Status of Mothers and Babies.

Year.	Number of Cases.	Rh Status of Babies of Rh-Negative Mothers.				
		Total Number of Rh-Negative Mothers.	Rh-Negative.	No Test (Stillborn).	Rh-Positive.	Maternal Serum with Antibodies.
1946	1996	316	131	1	184	12 (3·8%)
1947	2266	387	165	3	219	9 (2·3%)
1948	2284	369	141	3	225	23 (6·2%)
1949	2987	512	187	1	324	27 (5·3%)
Total	9533	1584	624	8	952	71

plete antibodies can pass the placental barrier, these (in the same or a lower titre than that of the agglutinating type) must also have been present in the maternal serum. In a few instances in which the test described by Wiener and Hardman (1948) for detection of incomplete antibodies masked by strong agglutinating antibodies has been carried out, the presence of the former has been demonstrated.

In the cord serum of Rh-positive babies, titres were not directly related to those in the maternal serum, variable amounts presumably being absorbed on to the specific receptors of the infants' cells.

In Rh-negative babies, on the other hand, whose cells lack the specific receptors, incomplete antibodies found in the cord blood were of the same titre as those in the maternal blood. They may persist for some time, with gradual fall in titre. In one case described by Wiener (1948) they could be demonstrated four months after birth.

Time of Appearance of Rh Antibodies in Maternal Serum.

Moureau (1949) has examined the red cells of aborted fœtuses, but while confirming the finding of Kemp (1930) that the A factor is developed as early as the thirty-seventh day, he could not demonstrate the D factor in forty-day fœtuses, but found it at the sixtieth day. He also found that the C and E factors were absent at the sixtieth day but could be identified in ninety-day-old fœtuses.

From these observations it can be concluded that Rh antibodies present in the maternal serum before the end of the eighth week of pregnancy were probably due to previous stimulation, either by an earlier pregnancy or by transfusion with Rh-positive blood.

In our series, 12 of the 71 patients were examined prior to the ninth week. Among these, Rh antibodies (all containing anti-D) were found in eight instances, and in all of these there was at least a suggestive history (based on clinical findings in regard to those patients whom we had not had opportunity to test in earlier pregnancies) or serological evidence of previous stimulation. In the four cases in which antibodies could not be demonstrated in the patient's serum at or before the eighth week, there was no clinical evidence of previous stimulation. The details of these 12 cases are shown in Table III. In one woman (Case IX) antibodies had been present in very weak titre at the time of delivery of her first child, which was clinically unaffected (being born in 1945, it is not included in our series). Her second pregnancy occurred during the period under review. No antibodies were demonstrable in her serum when examined during the second month, but they developed later. The second child had *icterus gravis*, requiring a blood transfusion. In another case (Case X) we have no serological data about the first pregnancy; antibodies developed only during the later months of the second pregnancy, but the fœtus was stillborn with characteristic features of congenital œdema. In both these cases, in which, at the most, very slight or perhaps (in Case X) no sensitization of the mother occurred during the first pregnancy, there was well-developed disease in the child of the second pregnancy. We have not sufficient data to fix the time of first appearance of antibodies in these two women; in Case IX no examination of the mother was made after the second month until delivery, when there were traces of agglutinating and strong incomplete antibodies, the latter to a titre of 120. The patient in Case X was reexamined during the ninth month, at which time, and at delivery, incomplete antibodies were present to a titre of 64.

The correlation of clinical history and serological tests in these 12 cases is in accord with the findings of Moureau cited above. Among the other patients in our series, not examined until after the second month, there is one instance in which antibodies were present as early as the tenth week of the second pregnancy. In this case there was no clinical or serological evidence of previous stimulation. The child was born at term, it became moderately jaundiced and anæmic, and required one blood transfusion. At the other extreme, there was a case in which antibodies were not demonstrable until the tenth day of the puerperium following the second pregnancy. This woman's first pregnancy had terminated in a miscarriage during the third month. The child of her second pregnancy developed anæmia requiring blood transfusion seventeen days after birth, although the Coombs test and tests for antibodies in the cord blood had produced negative results; during her third pregnancy incomplete antibodies were present at her first ante-natal visit (during the fourth month) and the baby was stillborn (six weeks prematurely) with congenital œdema. In this case it is difficult dogmatically to ascribe the anæmia which occurred in the second child to Rh incompatibility, since the maternal immunization was apparently too mild at the time of its birth to sensitize its cells; there were, however, no other obvious factors to which the anæmia could be ascribed.

TABLE II.
Antibodies in Maternal Serum.

Type of Antibody Demonstrated.	Number of Cases.	Comments.
Agglutinating only	9	No titre higher than that obtained with saline cell suspensions was obtained by the indirect Coombs test. In all cases, red cells from the cord blood gave positive reactions to the direct Coombs test, and in most, free incomplete antibody could be detected in the cord serum.
Incomplete only	47	No agglutination occurred of cells suspended in saline.
Both types present	15	The titre obtained by the indirect Coombs test was higher than that obtained with saline suspensions of cells.
Total ..	71	

In contrast, there were several instances in this series of sensitization of the child's red cells, as indicated by positive Coombs reactions, without accompanying clinical manifestations.

We have encountered a case (not in this series) in which incomplete antibodies were demonstrable a week after the second of two miscarriages at twelve weeks, occurring within six months of each other. This would appear to be evidence that early miscarriage can stimulate the production of maternal antibodies and give rise to the likelihood that future children may be affected; but it must not be taken as confuting the statistical evidence of Levine (1948) and others that such early miscarriages are not themselves attributable to Rh incompatibility.

We attempted to ascertain whether there was any broad correlation between the appearance of antibodies before and after the first twenty weeks of pregnancy and the incidence and severity of clinical *erythroblastosis fœtalis* in the child. Suitable data were available in respect of 44 cases, and the results are shown in Table IV. The figures would, on face value, suggest that the earlier appearance of antibodies had an adverse effect on the infantile mortality rate, but statistical analysis reveals that the differences shown are not in themselves significant, though they may be indications requiring confirmation.

In two cases in which the babies were Rh-negative there was a history of maternal blood transfusion, and although it is not known for certain that these Rh-negative women had been given Rh-positive blood, it seems likely that this is the explanation of the presence of antibodies in their serum, as there was no record of *erythroblastosis fœtalis* in earlier children as a possible cause of their stimulation.

In one case encountered too recently for inclusion in this series, the mother's serum contained no antibodies at the time of her first ante-natal visit, but at the time of

TABLE III.

Details of 12 Cases in which the First Examinations of Maternal Blood were Made Prior to the Third Month.

Case Number.	Parity.	Results of Previous Pregnancies.	Rh Antibodies in Maternal Serum.				Rh Antibodies in Cord Serum.		Coombs Test Result (Cord Cells).	Clinical Condition of Child up to 14th Day.	Notes.
			Before 60th Day.		At Delivery.						
			Type.	Titre.	Type.	Titre.	Type.	Titre.			
I. (Mrs. Ro., 1948).	2	Ectopic pregnancy five years earlier.	Incomplete anti-D.	32	Incomplete anti-D.	32	Incomplete anti-D.	32	Negative.	Normal.	Mother and child both belong to sub-type Rh'. Antibodies due to transfusion at time of first pregnancy.
II. (Mrs. Gi., 1947).	3	First child normal; second child died (cause unknown).	Incomplete anti-D.	Not estimated.	Incomplete anti-D.	2000	Incomplete anti-D.	120	Positive.	*Icterus gravis*, died fourth day.	Mother transferred 15 months prior to third pregnancy.
III. (Mrs. Bo., 1948).	3	First child normal; second child died (*icterus gravis*).	Agglutinating anti-D.	64	Agglutinating anti-D.	250	Incomplete anti-D.	32	Positive.	*Icterus gravis*, two transfusions.	Agglutinating titre was 64 at eight months; rose to 2000 ten days after delivery.
IV. (Mrs. Hau., 1948).	4	First child stillborn (see note); second child normal.	Agglutinating anti-D.	8	Agglutinating anti-D.	16	Incomplete anti-D.	8	Positive.	*Icterus gravis*, one transfusion.	First baby's stillbirth attributed to prolapsed cord. Fifth baby born in 1950, therefore not included in review, has shown no clinical manifestations of *erythroblastosis fœtalis*.
	5		Agglutinating anti-D.	2	Agglutinating anti-D.	8	Incomplete anti-D.	Trace.	Positive.	Normal.	
V. (Mrs. Mu., 1949).	5	First to third children normal; fourth, miscarriage.	Agglutinating anti-D.	4	Agglutinating anti-D.	4	Incomplete anti-D.	Trace.	Positive.	Normal.	
VI. (Mrs. Du., 1947).	5	First and second children normal; third, miscarriage; fourth, *icterus gravis*, recovered.	Agglutinating anti-D.	4	Agglutinating anti-D.	4	Incomplete anti-D.	Trace.	Positive.	*Icterus gravis*.	
VII. (Mrs. In., 1948).	8	First to sixth children normal; seventh, late anæmia.	Agglutinating anti-D.	4	Agglutinating anti-D.	4	Not detected.		Test not made.	Normal.	In seventh pregnancy first examination was at three months, when no antibodies were detected. Present at eight months (titre not estimated). At delivery 64. Coombs test positive result in cord blood.
VIII. (Mrs. Da., 1949).	14	First to eighth children normal; ninth to eleventh, ? affected; twelfth child affected; thirteenth, miscarriage.	Agglutinating anti-D.	120	Agglutinating anti-D.	64	Incomplete anti-D.	64	Negative.	Normal.	Baby Rh-negative.
IX. (Mrs. Hu., 1948).	2	First child normal (see note).	None.		Agglutinating anti-D.	120	Incomplete anti-D.	2	Positive.	*Icterus gravis*, two transfusions.	Trace of antibody present in maternal serum at delivery of first child (1945).
X. (Mrs. Har., 1948).	2	First child, no record.	None.		Agglutinating anti-D.	64	Present.	Not estimated.	Test not made.	Stillborn, macerated.	Cord blood too hæmolysed for titre and Coombs test.
XI. (Mrs. Bu., 1946).	2	First child, no record.	None.		Agglutinating anti-D.	64	Not tested.	Not estimated.	Test not made.	*Icterus gravis*, three transfusions.	
XII. (Mrs. Wl.)	3	First and second children normal.	None.		Agglutinating anti-D. Incomplete anti-D.	16 120	Incomplete anti-D.	4	Positive.	*Icterus gravis*.	No antibodies in maternal serum at sixth month.

TABLE IV.

Relationship between Early Appearance of Maternal Antibodies and Disease in Infants.

Previous History of Maternal Blood Transfusions or *Erythroblastosis Fœtalis* in Earlier Children.	Antibodies Present Before Twentieth Week.					Antibodies Not Present until After Twentieth Week.				
	Baby Rh (D)-Positive.[1]				Baby D-Negative.	Baby Rh (D)-Positive.[2]				Baby D-Negative.
	Clinical *Erythroblastosis Fœtalis.*			Not Clinically Affected.		Clinical *Erythroblastosis Fœtalis.*			Not Clinically Affected.	
	Died.		Recovered.			Died.		Recovered.		
	Still-birth.	Neo-natal Death.				Still-birth.	Neo-natal Death.			
Erythroblastosis fœtalis in previous babies	1	1	6	—	—	—	—	4	1	—
No *erythroblastosis fœtalis* in previous babies	2	1	3	5	—	2	—	11	6	—
Maternal blood transfusions	—	—	—	—	2	—	—	1	—	—
Totals	5		9	5		2		16	7	—

[1] Among 19 Rh-positive babies, the number affected was 14 (73·7%), the total mortality was five (26·3%), and the mortality in affected babies was 35·7%; a history of *erythroblastosis fœtalis* in earlier siblings was obtained in 42·1% of cases. The difference (26·3% less 8·0%) in the total mortality is not statistically significant ($P = 0·11$). The difference (35·7% less 11·1%) in the mortality in affected babies is not statistically significant ($P = 0·11$). The difference (42·1% less 20·0%) in the histories of *erythroblastosis fœtalis* in previous siblings is not statistically significant ($P = 0·10$).

[2] Among 25 Rh-positive babies, the number affected was 18 (72·0%), the total mortality was two (8·0%), and the mortality in affected babies was 11·1%; a history of *erythroblastosis fœtalis* in earlier siblings was obtained in 20% of cases.

delivery of twins at about the twentieth week her serum contained incomplete antibodies to a titre of four, with a subsequent rise to 64 on the ninth day of the puerperium. Both twins were Rh-positive, but their response to the Coombs test was negative and no free antibodies could be detected in their cord blood. This finding raises the question whether the placenta, though obviously allowing the antigen to pass from fœtus to mother, likewise equally allows transference in the reverse direction, of antibodies from maternal to infantile circulation, at whatever stage of pregnancy they are formed. Wiener (1948) has demonstrated their presence in the cord blood of a baby born at the thirty-fourth week, but apart from this observation little is known concerning the time factor in the passage of Rh antibodies across the placenta in man. It is possible that the histological condition of the human placenta during the earlier stages of pregnancy is such that, at least to some extent, it prevents or lessens the transference of maternal antibodies. There is also the possibility that some fœtal or maternal physiological neutralizing function is more actively operative during the earlier than in the later stages of pregnancy.

Incidence of Erythroblastosis Fœtalis in Successive Pregnancies.

The incidence of *erythroblastosis fœtalis* in the pregnancies under review in our series is shown in Table V.

As would be expected, in view of the average size of present-day families, a large proportion of the women in our series have had not more than four pregnancies.

We have, for the purpose of analysis, arbitrarily divided our series of 71 cases in which antibodies were present in maternal serum into two groups: (i) those coming under review in the first to fourth pregnancy; (ii) those coming under review in the fifth to fourteenth pregnancy.

As is shown in Table VI, the relative incidence of and the mortality from *erythroblastosis fœtalis* are approximately equal in each group, a finding somewhat at variance with the usual conception that *erythroblastosis fœtalis* tends to become progressively worse with each succeeding pregnancy.

Our series of 71 pregnancies in which antibodies were found in the maternal serum occurred in 65 women; there were five instances in which the same woman had more than one pregnancy during the period under review (second

TABLE V.

Rh Status of Babies, and Clinical or Post-mortem Findings in those which were Rh-Positive, in 71 Cases in which Maternal Serum Contained Rh Antibodies.

Parity of Mother.	Number of Cases.	Baby Rh-Positive.				Baby Rh-Negative or D-Negative.
		Post-Mortem or Clinical Evidence of *Erythroblastosis Fœtalis.*			No Signs or Symptoms of Erythroblastosis.	
		Fatal Erythroblastosis.		Non-Fatal Erythroblastosis.		
		Prenatal.	Neonatal.			
1	2		1		1	
2	20	2	1	12	4	1 (rh′)
3	18	3	1	9	3	1 (rh″)
4	12	2		9	1	
5	7	1		2	2	2
6	2			1		1
7	3			3		
8	3	1			1	1
10	1			1		
11	1	1				
13	1			1		
14	1					1
Total	71	13		39	12	7

TABLE VI.

Comparison between Incidence and Mortality of Erythroblastosis Fœtalis *in Rh-Positive Babies Born of Earlier (First to Fourth) Pregnancies and Later (Eighth to Fourteenth) Pregnancies.*

Group.	Number of Cases.	Incidence of *Erythroblastosis Fœtalis.*		Fœtal or Neonatal Deaths Attributable to *Erythroblastosis Fœtalis.*		
		Total Number of Cases.	Percentage.	Number.	Percentage of Affected Babies.	Percentage of Total Babies.
I. (First to fourth pregnancy)	50	41	82·0	10	24·4	20·0
II. (Fifth to fourteenth pregnancy)	14	11	78·6	3	27·3	21·4
Total	64	52	81·25	13	25·0	20·3

and third, fourth and fifth, seventh and eighth, and eleventh and thirteenth each once, and third, fourth and fifth in one case).

If we compute for these 65 women their total number of pregnancies, including both those which occurred during the period under review and those prior to it, it will be found that in Group I there were 48 women who had had collectively 131 pregnancies, and in Group II, 17 women with a total of 122 pregnancies. The incidence of *erythroblastosis fœtalis*, and the mortality (both over-all and per affected babies) in respect of the total pregnancies in each group (as based on clinical evidence in cases in which serological data were not available) are shown in Tables VII and VIII. The available data suggest a higher incidence of *erythroblastosis fœtalis* in Group I than in Group II, the difference between them being statistically significant ($P < 0.001$). On the other hand, the differences between the case mortality and the over-all mortality in the two groups are not statistically significant.

Since analysis of the pregnancy under review in our series and analysis of the total number of pregnancies of the women concerned both revealed a higher incidence of *erythroblastosis fœtalis* in Group I than in Group II, it is pertinent to discuss some possible explanations of these unexpected findings.

1. In Group I, among the 47 children from whom blood samples were obtainable, only two were D-negative (that is, could be said with certainty to have heterozygous fathers), whereas in Group II, among 16 children tested, five were D-negative. These findings give a value for P of 0·01, which indicates a statistically significant higher proportion of fathers homozygous for the D factor in Group I. We consider that this incidence of homozygosity of the fathers, which would tend to result in more frequently repeated stimulation of the mothers, is the most likely explanation of the difference between the two groups. We do not know whether this difference is a chance distribution in our series, or whether on the other hand the successive births of affected children have led to voluntary prevention of further pregnancies. The latter possibility would in itself tend to diminish the proportion of homozygous fathers in our Group II.

2. Another factor we have examined is the possible influence of the so-called "competition of antibodies". The A B O relationship of mother and child has been determined in 56 cases (tests on the other eight being impossible owing to fœtal maceration), and it has been found that in this series as a whole "protective" incompatibility of A B O factors—that is, competition of antibodies—was present in only five (8·9%) as opposed to the normal incidence of 22·2% (Bryce, Jakobowicz, McArthur, 1946)—a difference which is statistically significant ($P = 0.02$). Of these five cases, two occurred in Group I, giving an incidence of about 4·4%, and three in Group II, an incidence of about 27·3%, a difference doubtfully weighted against Group I in respect of any protective influence which may be exerted by A B O incompatibility ($P = 0.047$).

If, as we think is correct, we assume that the unequal distribution in our two arbitrary groups is due only to the element of chance in a series of this size, nevertheless it

TABLE VII.

Number of Clinical Cases of Erythroblastosis F œtalis *in Babies of Latest and Previous Pregnancies of 65 Women with Rh Antibodies in Their Serum.*

Parity.	Number of Women.	Number of D-Negative Babies.	Cases of Erythroblastosis in Each Pregnancy, with Number of Fatal Cases Shown in Parentheses.												
			1st.	2nd.	3rd.	4th.	5th.	6th.	7th.	8th.	9th.	10th.	11th.	12th.	13th.	14th.
1	2		1 (1)													
2	19	1	0	15 (3)												
3	17	1	0	9 (2)	14 (4)											
4	10		0	1	7 (4)	9 (2)										
5	7	2	0	0	0	3	3 (1)									
6	2	1	0	0	1	1	1 (1)	1								
7	2		0	0	0	0	0	0	2							
8	3	1	0	0	0	1 (1)	1 (1)	1 (1)	1	1 (1)						
10	1		0	0	0	1	1	1	1 (1)	1	0	1				
13	1		0	0	0	0	0	0	1	1	2 (1)[1]	1	1 (1)	1 (1)	1	
14	1	1	0	0	0	0	0	0	0	0	1	1 (1)	0	1	0	0
	65	7	1 (1)	25 (5)	22 (9)	15 (3)	6 (3)	3 (1)	5 (1)	3 (1)	3 (1)	3 (1)	1 (1)	2 (1)	1	0

[1] This pregnancy resulted in twins, both affected with *icterus gravis*, one fatally.

TABLE VIII.

Incidence and Mortality of Erythroblastosis Fœtalis *in all Babies Born, both Before and During the Four-Year Period Reviewed, to the 65 Women whose Serum Contained Rh Antibodies.*

Comparisons.	Number of Women.	Total Number of Pregnancies.	Incidence of *Erythroblastosis Fœtalis.*		Mortality from *Erythroblastosis Fœtalis.*		Percentage of Total Pregnancies.
			Number of Cases.	Percentage.	Number of Deaths.	Percentage of Affected Cases.	
Group I	48	131	56	42·7	16	28·6	12·2
Group II (first to fourth pregnancies)	17	68	7	11·7	1	14·3	1·7
All first to fourth pregnancies	65	199	63	33·0	17	27·0	8·9
Group II (first to fourth pregnancies)	17	68	7	11·7	1	14·3	1·7
Group II (fifth to fourteenth pregnancies) ..		54	27	50·0	10	37·0	18·5
All cases in Group I..	48	131	56	42·7	16	28·6	12·2
All cases in Group II ..	17	122	34	27·9	11	32·6	9·2
Total	65	253	90	35·4	27	30·0	10·7

and the presumably equally fortuitous difference in the distribution of homozygous fathers in our two groups illustrate the need for caution in the interpretation of findings such as those presented in this series.

However, in spite of this need for caution, there is no doubt that individual cases in this series illustrate the fact that the disease does not always become progressively more severe in succeeding pregnancies.

One interesting example is that of Case IV in Table III; the first child of this woman was stillborn, presumably because of a prolapse of the cord, the second was normal, the third died of severe *icterus gravis*, the fourth was affected with *icterus gravis* but recovered after one blood transfusion, the fifth was clinically normal. All the children, except the first, have been examined and are known to be Rh-positive, and the fourth and fifth are known to have given positive results to the Coombs test.

Another case of interest is that of Mrs. S., examined in her thirteenth pregnancy. She had had six unaffected children, followed by two with non-fatal *icterus gravis*. The ninth pregnancy resulted in the birth of twins, both affected with *icterus gravis*, one fatally and one with recovery. The tenth baby had non-fatal *icterus gravis*, the eleventh and twelfth were stillborn, hydropic and macerated, but the thirteenth, although affected with *icterus gravis*, recovered.

Summary.

1. The results are presented of serological examination of a consecutive series of 9533 mothers and babies in relation to Rh incompatibility.

2. In this series of women 1584 (16·7%) were Rh-negative.

3. Of these Rh-negative women 952 had Rh-positive babies and eight had stillborn babies who could not be tested but were presumed to be Rh-positive, making a total of 960 (60·6%).

4. Rh antibodies were found before, at or after delivery in the serum of 71 (4·5%) of all the Rh-negative women in this series, and 6·7% of those with Rh-positive babies.

5. The types of antibody found, the time of their appearance in the maternal serum, and the relationship of the time factor to infantile *erythroblastosis fœtalis* are discused.

6. The incidence of *erythroblastosis fœtalis* in relation to parity, and possible factors influencing this incidence, have been reviewed and statistically analysed.

II. CLINICAL ASPECTS.

(K.C.)

Of the 71 infants in this series, 10 were stillborn and 61 were born alive. Of the latter, 42 were affected to a greater or less degree. Thus 52 (that is, 73·2%) of the total were affected, and 19 (26·7%) were unaffected. The Rh status of the 61 liveborn infants is shown in Table IX.

Of the 10 stillborn infants, two were Rh_0 (D) positive, and it is assumed that the remaining eight, who were too macerated to permit of blood tests, were also Rh_0 (D) positive.

In the entire series of 71 infants we may therefore take it that 64 (90%) were Rh_0 (D) positive and seven (10%) were Rh_0 (D) negative.

TABLE IX.

The Rh Status of the 61 Liveborn Infants.

Group.	Number of Cases.
Rh_0 (D) positive	54
Rh_0 (D) negative	7
Rh negative 5	
D negative (rh') 1	
D negative (rh") 1	

Of the 64 Rh_0 (D) positive infants, 52 (81%) were affected and 12 (19%) were unaffected.

The 19 unaffected infants are therefore composed of 12 Rh_0 (D) positive and seven Rh_0 (D) negative infants.

Type of Erythroblastosis Fœtalis.

In the series of 52 affected infants 10 were stillborn and 42 liveborn. As is shown in Table II, *icterus gravis* was much the commonest manifestation (36 cases), then followed congenital œdema of the fœtus (10 cases), anæmia without jaundice being an infrequent condition (five cases). In the case labelled "indeterminate", death from atelectasis occurred at six hours before clinical signs of *erythroblastosis fœtalis* were obvious, and post-mortem examination showed that the condition was present.

Prematurity.

The incidence of prematurity in the average population is generally taken as about 6% to 10%. In this series it was as shown in Table XI.

It will be seen (Table XI) that while the incidence of prematurity among the unaffected infants is about the same as that of the average population, among the affected infants it is higher, and also that the more severe the manifestation of the disease, the greater is the incidence of prematurity. This is, of course, a well-recognized fact noted by all observers.

The Sex Incidence.

As shown in Table XII the over-all sex incidence is the same. The figures in the individual manifestations, small though the series is, agree with the findings of Gilmour (1944) in the greater incidence of congenital œdema in females, and the preponderance of *icterus gravis* in males.

TABLE X.
Incidence of Different Manifestations of Erythroblastosis Fœtalis.

Manifestation.	Number of Cases.	Percentage of Affected Infants.	Percentage of Total Rh-positive Infants.
Congenital œdema of fœtus ..	10	19·2	15·4
Icterus gravis	36	69·2	55·4
Anæmia without jaundice	5	9·6	7·7
Indeterminate	1	1·9	1·5
Total	52	—	—

The Fate of the Affected Infants.

The fate of the 52 affected infants is shown in Table XIII.

It is apparent therefore that there was a "fœtal wastage" (combined stillbirths and neo-natal deaths) of 27%. Of this wastage the bulk was due to stillbirth, and the remainder of deaths were neo-natal.

TABLE XI.
Incidence of Prematurity.

Subjects.	Number of Cases.	Premature.	Full Term.	Percentage Premature.
Unaffected infants	19	2	17	11·5
Affected infants:				
Congenital œdema of fœtus	10	6	4	60·0
Icterus gravis	36	4	32	11·1
Anæmia	5	—	5	0
Indeterminate	1	—	1	—
Total	52	10	42	18·8

The Four Neo-Natal Deaths.

It must be borne in mind that any series of newborn infants, besides being at risk from the particular condition under consideration, is also subject to the usual hazards and ills of the newborn infant in general. Therefore an infant with fœtal erythroblastosis may also suffer from some other condition which is the cause of death.

CASE I.—The mother was confined for the third time; she was of blood group O, Rh-negative. The first child was unaffected, and the second died. The history was unobtainable. The mother had been given a blood transfusion after the birth of the second child. In the third pregnancy incomplete antibodies were detected in the blood at two months, and at delivery the titre was 1 in 2000. The infant was a female (Baby 21: Glb.), slightly premature, the gestation being 37·5 weeks, and the child's length 19 inches and weight six pounds one ounce. Its blood group was O and the Rh factor reacted only with Rh′ sera. The cord blood contained incomplete antibodies (1 in 120) and the Coombs test result was positive, indicating that the receptors to anti-Rh_0 were completely blocked. Jaundice appeared at twelve hours and the following day was deep. The spleen was palpable. The red blood cell count was 5,200,000 per cubic millimetre and the hæmoglobin value 110% (15·4 grammes *per centum*). On the third day the red cell count was 4,900,000 per cubic millimetre and the hæmoglobin value was 100% (14 grammes *per centum*). The jaundice increased and the temperature rose to 102·8° F. Early on the fourth day there was a sudden onset of dyspnœa, universal crepitations being heard throughout both lungs, and the baby died one and a half hours later.

Post-mortem examination revealed several small subpleural hæmorrhagic spots, the lungs being otherwise normal on macroscopic examination. Examination of the brain revealed bile staining of the basal ganglia. Death was considered to be due to *icterus gravis* and kernicterus with associated failure of the pulmonary circulation.

TABLE XII.
Sex Incidence.

Subjects.	Male.	Female.
19 unaffected infants ..	10	9
52 affected infants: ..	27	25
10 with congenital œdema of fœtus	4	6
36 with *icterus gravis* ..	21	15
5 with anæmia	3	2
1 with an indeterminate manifestation ..	—	1

CASE II.—Baby 27 (Hal.) was an "emergency case", admitted to hospital when three days old. The mother was a *primipara* and had had no previous miscarriages or blood transfusions. She was of blood group O, Rh-negative, and at five days after delivery had agglutinating antibodies to a titre of 1 in 16. The infant was a full-time male with a birth weight of seven pounds two ounces. The jaundice appeared at two hours. On admission to hospital the infant was deep golden yellow in colour and listless, with a subnormal rectal temperature (96·4° F.). There was pitting œdema of the hands and feet in which the hypothermia may have played a part. The liver was enlarged to the level of the umbilicus and the spleen reached almost to the umbilical level. The urine contained bright blood. Head retraction was absent. The red cell count was 1,300,000 per cubic millimetre and the hæmoglobin value was 36% (five grammes *per centum*). The infant was given a transfusion of rh-negative blood, two millilitres of "Campolon" intramuscularly, and injections of vitamin *K* analogue. The following day the red cell count rose to 5,800,000 and the hæmoglobin value to 120% (16·8 grammes *per centum*). On the next day (the fifth) the infant became more listless, developed head retraction, passed blood in the urine and stools, and died.

TABLE XIII.
Analysis of Fate of 52 Affected Infants.

Subject.	Number.	Percentage of Total.	Mortality.		
			Number.	Percentage of Total Affected.	Percentage of Liveborn Infants.
Stillborn	10	19·2	10	19·2	—
Liveborn	42	80·8	4	7·7	9·5
	52		14	26·9	

At post-mortem examination the pleura of the lungs was found to be blotchy, the lung substance being firm and fleshy. No hæmorrhages were seen on macroscopic examination. Microscopic examination revealed some areas of distended alveoli with ruptured walls. The collapsed areas were congested and some pigmentation was seen in them. Some bronchi contained red blood cells. There were many macroscopically evident areas of hæmorrhage in the wall of the jejunum and the ileum, and a small amount of blood was present in the lumen of the small intestine. The gastric mucosa was congested. Examination of the suprarenals revealed a congested medulla with much altered blood pigment. The basal ganglia of the brain were bile-stained, and the vessels in the white matter were congested. Death was considered to be due to *icterus gravis* and kernicterus with severe hæmorrhagic manifestations.

CASE III.—The mother was confined for the third time, and was aged thirty-nine years. The first pregnancy had resulted in an unaffected female child, one month premature, who survived. The second child died at two days with jaundice, and no further details of this were obtainable. The mother gave a history of thyreoid enlargement and exophthalmos since the age of fifteen years, and had at one time been treated with Lugol's solution. Eleven days prior to the birth of the third infant (Baby 14: Hen.), she was found to have a blood pressure of 160 millimetres of mercury, systolic, and 95 millimetres of mercury, diastolic, and tachycardia. She was admitted to hospital for observation by the physician. The tachycardia subsided and she was found to have no evidence of thyreotoxicosis. She came into labour at thirty-five weeks' gestation, and four hours later gave birth to an infant 19 inches long, weighing seven pounds seven ounces. Unfortunately no note was made as to the condition of the placenta, except that it was complete. At birth the infant had the characteristics of a premature baby and was noted to be "mucusy". It had inhaled much thickly meconium-stained liquor. It was cyanosed, and was given penicillin and oxygen and vitamin *K*. Slight jaundice was noted "shortly after birth", and there were bruises on the skin. At seventeen hours the jaundice was pronounced.

On the first day the infant's hæmoglobin value was 95% (13·3 grammes *per centum*). On the following day the jaundice was more pronounced, the infant was sluggish, its spleen was palpable and the ecchymoses were more obvious. The red cell count was 2,900,000 per cubic millimetre and the hæmoglobin value was 76% (10·6 grammes *per centum*). The infant was given a transfusion of Rh-negative blood. On the third day the red cell count was 4,300,000 per cubic millimetre, and the hæmoglobin value was 105% (14·7 grammes *per centum*); some œdema of the legs was noted.

On the fourth day there was some nasal discharge; the blood count was stationary, the jaundice was still deep and the ecchymoses were disappearing. Gross chest retraction was still present, and the infant was cyanosed unless given continuous oxygen.

On the sixth day the infant passed several fluid green stools which on culture yielded no pathogens. The hæmoglobin value was 118% (16·5 grammes *per centum*), the rise in the hæmoglobin value probably being associated with some fluid loss in the stools.

On the seventh day the hæmoglobin value was the same, and there was some bile-stained vomitus. The respirations became grunting, the cyanosis increased and crepitations were heard over the upper lobes of both lungs. Clinically the picture was that of clearing *icterus gravis* with post-atelectatic bronchopneumonia complicated by diarrhœa, perhaps associated with the rhinitis. The penicillin dosage was increased and the infant was given "Coramine", but died in a few hours.

At post-mortem examination the lungs were found to be affected by irregular patchy consolidation. Microscopic examination revealed many hæmorrhages, the non-air-containing lung alternating with over-distended air-containing alveoli. The liver was enlarged and dark in colour. Pronounced erythropoiesis was evident with clear-cut connective tissue in the portal tracts. The spleen was enlarged, and a depressed infarct was found in the central third. The heart was normal and contained no thrombi. In the pancreas some fibrous and fatty tissue was found between the lobules. In the islets a few cells had very large nuclei. The small intestine contained thin, semi-fluid material.

This case shows several interesting features. The mother evidenced moderate hypertension. The infant's length of 19 inches is excessive for the estimated period of gestation of thirty-five weeks. One would expect a length of 17·5 inches. Also the weight of seven pounds seven ounces is excessive for a length of 19 inches, for which one would expect a weight of five and a half pounds. Although the œdema was not specifically noted till the third day, it is legitimate to assume that the infant must have been œdematous at birth. The fact that the liquor was thickly stained with meconium and that the infant had inhaled some prior to a normal four-hour labour, indicates some degree of intrauterine anoxæmia. This is not infrequently seen in ordinary fœtuses of mothers with such a degree of hypertension as this mother exhibited, and is probably due to some degree of impairment of placental function in these cases. This infant at birth therefore suffered from *icterus gravis* and atelectasis.

The subsequent progress of this baby was that of a baby with *icterus gravis* who had survived the first five days, which is the critical period for this disease, and who was in the recovery phase. On the fourth day it developed rhinitis and on the sixth day non-specific diarrhœa. On the seventh day rapidly fatal bronchopneumonia occurred, lasting only a few hours.

The pulmonary picture throughout was that of atelectasis as distinct from the picture of the pulmonary œdema which is so often the terminal event in kernicterus. The absence of inflammatory reaction in the lung was regarded as due to the very short duration of the pneumonia —four hours— *plus* the penicillin therapy. Although this case is included among the deaths from fœtal erythroblastosis, one assesses the immediate cause of death as atelectasis in a premature infant of a moderately hypertensive mother. The *icterus gravis* is not regarded as the actual cause of death.

CASE IV.—The mother was aged forty years, and had previously had two unaffected infants. At four months' gestation in her third pregnancy she was in hospital for three weeks with threatened miscarriage—pain and vaginal hæmorrhage. She was admitted to hospital again with similar symptoms at five and a half months. She showed mild toxæmia and hypertension (systolic blood pressure 160 millimetres of mercury, diastolic pressure 100). At term she was given medical stimulation on two occasions with no result. The membranes were then stripped and she came into labour at forty-one weeks. Her blood group was A (subgroup A_1), Rh-negative. There were no antibodies at four months of pregnancy. She showed incomplete antibodies, 1 in 64 at delivery and 1 in 128 at ten days. She had a seven-hour labour and was delivered of a female infant (Baby 12: Haw.) weighing seven pounds thirteen ounces, with a length of 20·5 inches. Examination of the placenta revealed many infarcts. The infant's condition appeared satisfactory at birth, but one hour later she was noted to be breathing irregularly and to be pale. In spite of oxygen, "Anacardone" and "Lobeline" therapy she died at five hours.

At post-mortem examination large, dark, blood-stained areas were seen on the surface of both lungs, varying from half to three-quarters of an inch in diameter. These were depressed below the surface of the air-containing lung. The trachea and bronchi were clear. On microscopic examination some alveoli were seen to contain debris from amniotic fluid. Areas of atelectasis and of hæmorrhage were also present. In the liver areas of erythropoiesis were present throughout. The spleen was congested. In the brain blood staining of the pre-arachnoid was seen, but there was no free blood in the skull.

The pathologist's conclusion was that death had occurred from atelectasis in an infant showing fœtal erythroblastosis. The cause of the atelectasis I regard as the unhealthy and greatly infarcted placenta, associated with the previous threatened abortions and the mild toxæmia. I do not think the fœtal erythroblastosis was the cause of death.

If we omit this last case, the neo-natal death rate due to fœtal erythroblastosis in the 52 affected infants becomes three (5·8%) or 7% of the 42 live births. Two of these three infants were under thirty-eight weeks' gestation.

Analysis of the 36 Cases of Icterus Gravis.

The 36 cases of *icterus gravis* were graded into three categories—severe, moderate and mild.

A case was regarded as severe if either the jaundice or the anæmia or both were severe. If the infant showed cerebral signs or was toxæmic, it was included in this group. The anæmia was considered severe if the hæmoglobin value fell to or below 60% (8·4 grammes *per centum*), and if after blood transfusion sufficient to raise the hæmoglobin to 100% (14 grammes *per centum*) it again fell to this figure. The "moderate" group included those with moderate jaundice or anæmia who were free of toxic and cerebral signs. The anæmia was considered moderate if the hæmoglobin value fell to 60% to 70% (8·4 to 9·8 grammes *per centum*), but responded to one blood transfusion. The "mild" group consisted of infants with mild jaundice generally of short duration with mild or late anæmia. Twenty-one cases (58·3%) were severe, eight (22·2%) moderate, and seven (19·4%) mild.

The time of onset of the jaundice was difficult to determine in some cases, as the infant had yellow vernix. It varied from within half an hour of birth to two days after birth.

The duration of the jaundice did not correspond with the severity. In the "severe" group it varied from three to twenty-eight days, and in the "mild" group from two to twenty-seven days.

Blood counts were made daily till the blood became stabilized, and then less often. There is frequently a dissociation between the anæmia and the jaundice. It would appear that the jaundice is determined by the hepatic efficiency. Some very grossly icteric infants are not anæmic. Conversely, in the type of fœtal erythroblastosis without jaundice the anæmia may be gross.

There were three deaths in this series giving a mortality of 8·3%. They occurred in Cases I, II and III, previously described.

The Incidence of Kernicterus.

It is possible that mild and transient cerebral symptoms may be missed in the first few days and that only the more severe cases are noted. Therefore the incidence of kernicterus in any series will vary with the standards taken and the closeness of observation. We have listed as suffering from kernicterus any baby who in the first week showed any cerebral signs such as undue drowsiness, irritability, restlessness, twitching, cerebral cry, head retraction or spasticity, in whom cerebral injury due to birth trauma could reasonably be excluded.

Included in the category of kernicterus also are those babies who in the follow-up examination showed evidence of damage to the cerebral nervous system.

Four cases of early kernicterus were noted, of which two were the fatal Cases I and II quoted above. The other two infants survived. One surviving infant (a full-term male) suffered from severe *icterus gravis* with obvious jaundice apparent almost at birth. He had gross head retraction and acute pulmonary œdema from which he recovered. Opisthotonos persisted for many weeks and he is now, at the age of nine months, spastic.

The fourth infant, also a full-time male, had severe *icterus gravis* with drowsiness on the second day and some twitching on the third day.

There were thus four infants (11%) who showed early kernicterus.

It is too early to determine if any of the other infants will show late kernicterus. They are being kept under observation.

Blood Transfusions.

All these infants were given simple blood transfusions. The transfusion level was taken as 3,000,000 red cells per cubic millimetre or a hæmoglobin value of 60% (8·4 grammes *per centum*). Twenty-six of the babies required blood transfusions. This included all those severely and moderately affected with three exceptions—one severely and two moderately affected. The infant (Case I—"severe" group) with fatal kernicterus had a hæmoglobin value of 100% (14 grammes *per centum*) and 4,000,000 red blood cells per cubic millimetre on the third day. The two moderately affected infants who did not require blood transfusion exhibited gross jaundice but only mild anæmia. None of the mildly affected infants required blood transfusion. The transfusions were all of Rh-negative blood, given by the drip method at the rate of as many drops per minute as the infant weighed in pounds. The amount given was based on the following formula: 100 – baby's percentage hæmoglobin value × baby's blood volume ÷ 100; the blood volume was taken as two ounces per pound of body weight. The blood given was in most instances obtained from the Red Cross Blood Transfusion Service, both male and female donors being used. It is estimated that the proportion of male to female donors is about equal.

Twelve infants required one blood transfusion, 10 required two transfusions, three required three transfusions, and one required six transfusions (four in the first twelve days, one at five weeks and another at six weeks).

The infants are watched in the follow-up clinic and the blood examinations are carried out as a routine until they reach the age of nine weeks. The early anæmia in the first month is hæmolytic, but the late anæmia coming on in the second month appears to be due to faulty erythropoiesis, as is suggested by the case of the infant who required transfusions at four to six weeks. The exact mechanism of this failure is not clearly understood. It may be a direct effect of the antibodies on the erythropoietic tissue. It is interesting to note the demonstration by Reno, Scauffer and Krosnick (1949) that an intrauterine X-ray film of a fœtus with fœtal hydrops revealed sclerosis of the bones with narrowing or obliteration of the medullary spaces.

Routine Treatment in Icterus Gravis.

The routine treatment employed in the *icterus gravis* cases was as follows. Injections of vitamin *K* analogue ("Menadione") were given daily, or more frequently, according to the severity of the jaundice and the presence of hæmorrhagic manifestations, during the period of severe icterus. Injections of two millilitres of crude liver extract (for example, "Campolon") were given once or twice weekly during the period of severe jaundice. Casein hydrolysate (25% solution) in amounts of one drachm per pound of body weight per day was added to the feeding, also a vitamin *B* complex preparation in amounts of 1·5 milligrammes of thiamine and riboflavine per day, and ascorbic acid (25 milligrammes per day). In the light of the investigation of Cathie (1947), which indicated that the antibodies in breast milk were not absorbed, breast milk was the routine feeding unless evidence of fatty intolerance developed. In such cases "Nestlé's Sweetened Condensed Milk" diluted one in eight was substituted.

Blood transfusions were given as previously stated when the red cell count fell to 3,000,000 per cubic millimetre (hæmoglobin value 60% or 8·4 grammes *per centum*).

In no case was labour induced early. It was considered that the risks of induction of labour and the burden of congenital disease on the immature organs outweighed the theoretical advantages. Recent work indicates that the kernicterus rate is high in infants born prematurely after induction of labour.

Anæmia without Jaundice.

There were five cases of anæmia without jaundice, the mildest manifestation of fœtal erythroblastosis. Three of these infants required blood transfusion. It is interesting to note that these transfusions were required at a later period than obtained in the *icterus gravis* series—namely, at thirteen days, three weeks and five weeks respectively. One has the impression that this anæmia is due more to failure of red cell production than to blood destruction. All five infants survived the neo-natal period. One infant died at a later date from congenital heart disease, but this case is not included in the deaths.

Correlation of Maternal Antibody Titres at Delivery with Clinical Findings in the Infants.

The type and titre range of antibodies in maternal serum at delivery and in cord serum are shown in Table XIV.

A hæmoglobin level in the first few days of 100% (14 grammes *per centum*) or more, and the absence of clinical evidence of fœtal erythroblastosis, were taken as standards of the infant's being unaffected.

The time of the appearance of the antibodies was as follows: present in maternal serum before seven months of pregnancy, seven cases; absent at the seventh month and present at delivery, three cases; absent at delivery and present ten days afterwards, two cases.

It will be noted that the titre is in general lower in the serum of mothers of unaffected infants than in the affected series.

The Coombs test on the cord blood produced a positive result in six cases, a negative result in one case (in which weak antibodies did not appear in maternal serum till ten days after delivery), and was not performed in five.

The distribution of titres in the blood of the mothers of the affected babies was as follows (Table XV).

The majority of mothers had an incomplete antibody titre of over 1:32, as compared with the mothers of unaffected infants, none of whom had a titre over 1:32.

TABLE XIV.

Subjects.	Antibodies in Maternal Serum.	Antibodies in Cord Serum.
Unaffected Rh-positive infants.	Incomplete: trace to 1:32.	Trace to 1:32.
Affected Rh-positive infants.	Incomplete: 1:2 to 1:2000. Agglutinating: 0 to 1:4000. (The infant of this mother was stillborn with congenital œdema.)	Trace to 1:128.

An analysis of the maternal blood antibody titres in the different types of fœtal erythroblastosis is as shown in Table XVI.

It will be seen that there is an over-all correlation between the severity of the infant's disease and the maternal antibody titre. In all cases of congenital œdema of the fœtus the titre was over 1:32. In *icterus gravis*, in 13 cases the titre was under 1:32, and in 23 it was 1:32

TABLE XV.

Type of Antibodies.	Titre.		
	Under 1:32.	1:32 to 1:128.	Over 1:128.
Incomplete	13	26	6
Agglutinating	42	6	3

or over. There was also a correlation between the severity of the *icterus gravis* and the titre. In four-fifths of the "severe" cases the titre was over 1:32, in half of the "moderate" cases it was over 1:32, and in three-sevenths of the "mild" cases it was over 1:32. Of the anæmia cases, in three the titres were designated "weak", and in two it was over 1:32, being 1:128.

TABLE XVI.

Infant's Condition.	Maternal Incomplete Antibody Titre.		
	Under 1:32.	1:32 to 1:128.	Over 1:128.
Congenital œdema of the fœtus: 10 cases ..	—	8	2
Icterus gravis: 36 cases—			
21 severe	5	12	4
8 moderate	4	3	1
7 mild	4	3	—
Total	13	18	5
Anæmia: 5 cases ..	3	2	—

Correlation of Incomplete Antibody Titre in Cord Blood with Severity of the Disease.

The highest titre (1:128) occurred in the cord blood of the infant who died of kernicterus. The next titre of 1:64 was found in a stillborn infant suffering from congenital œdema, though in congenital fœtal œdema the titre varies between 1:2, 1:8 and 1:64. Titres up to 1:32 were found indiscriminately in conditions ranging from mild anæmia to very severe *icterus gravis*.

Analysis of Titres in the Cases of Neo-Natal Death.

An analysis of the titres in the cases of neo-natal death is given in Table XVII.

In Case I the maternal and cord blood incomplete antibody titres were the highest in the series. In the emergency Case II the necessary information was not available.

Case III was that of the infant whose death was held to be due to atelectasis rather than to fœtal erythroblastosis, and the death in Case IV was also regarded as due to atelectasis. All that can be deduced is that in one case in which there was a most unusually high antibody titre, the infant died.

TABLE XVII.

Case Number.	Maternal Blood: Incomplete Antibody Titre.	Titre in Cord Blood.
Case I	1:2000.	1:128.
Case II	1:16 when infant 5 days old.	? (Emergency case).
Case III	1:64.	Trace.
Case IV	1:64.	1:16.

It would seem, therefore, that whereas in general it may be stated that a high antibody titre is more likely to occur with the more severe manifestations of the disease, this does not apply to the individual case. Therefore attempts to foretell the condition of any specific newborn infant from the maternal antibody titre are unreliable and misleading.

Correlation of "Peri-natal" Deaths (Combined Stillbirth and Neo-natal Deaths) with Histories of Previous Erythroblastosis in the Family.

In the 52 cases, one mother was *primipara* whose baby died of kernicterus (Case II). One was a virtual *primipara*, having had a previous miscarriage. In two cases accurate details of the previous pregnancies were unobtainable. In

TABLE XVIII.

Type of Fœtal Erythroblastosis in Previous Pregnancies.	Number of Cases.	Type of Fœtal Erythroblastosis in Present Pregnancy.			
		Congenital Œdema of Fœtus.	*Icterus Gravis.*		Late Anæmia without Jaundice.
			Baby Died.	Baby Recovered.	
Congenital fœtal œdema ..	—	—	—	—	—
Congenital fœtal œdema and *icterus gravis*	2	2			
Icterus gravis (fatal) ..	9	2	2	5	
Icterus gravis (non-fatal) ..	7	1	—	5	1
Anæmia without jaundice ..	1	1			
Total ..	19	6	2	10	1

the 48 remaining cases, 19 mothers gave a history of previous fœtal erythroblastotic infants, and 29 gave no history of previous fœtal erythroblastosis.

The outcome of the pregnancies in the 19 cases in which there was a history of previous erythroblastotic infants is presented in the following table (Table XVIII).

Of this series of 19 mothers with previous erythroblastotic children, 11 had lost previous children. In the pregnancy under consideration six out of the 11 infants died and five survived. Of the eight mothers in this series who

had not previously lost children, two lost babies in this pregnancy. Thus out of the series of 19 babies in this pregnancy eight died—42% peri-natal wastage.

Among the 29 mothers with no preceding history of fœtal erythroblastosis there were three fœtal deaths from erythroblastosis, all the infants being affected by congenital fœtal œdema—that is, peri-natal death of 10·3%.

In this series, therefore, it would appear that the infant of a mother with an erythroblastotic family history had a slightly better than even chance of surviving, and that with no previous erythroblastotic history the infant had a 90% chance of survival.

Difficulties in Accurate Evaluation of Therapy.

It is obvious that there is much spontaneous variation in the natural history of this disease. The delivery of a stillborn œdematous fœtus may be followed by the birth of a living child who survives. In this series there were twins with *icterus gravis*, one of whom died while one survived, both having the same treatment. It is this variability in the severity of the disease in different pregnancies and even in twins of the same pregnancy which makes it difficult to assess the value of any therapeutic procedure even when controls are used. The only real divergence of opinion in treatment at present is on the question of the type of blood transfusion—that is, whether replacement transfusion or "simple" transfusion is better. Accurate statistics with controls are needed to arrive at a conclusion.

Any figures from routine replacement transfusions at birth based on a positive response to the Coombs test alone will give figures which appear better than they actually are, because some infants who would not be clinically affected are included and treated. The replacement transfusion has the following disadvantages: (i) It is physiologically undesirable to replace the blood of the newborn infant with adult blood. One must, however, admit that in practice no observable harm is seen. (ii) Replacement transfusion is technically more difficult of performance than the "simple" transfusion and is also more time-consuming. (iii) It exposes the infant to the risk of death from overloading of the circulation, from shock, or from infection, all of which complications have occurred.

Since no infant now should die of the anæmia of fœtal erythroblastosis, the crux of the problem is whether by replacement transfusion the damage to the liver and brain can be prevented, as these are the killing and maiming conditions. There is an undoubted place for replacement transfusion in the treatment of those infants who at birth show such a gross grade of anæmia—for example, a hæmoglobin value of 20% to 30% (2·8 to 4·2 grammes *per centum*)—that it is impossible to give a transfusion large enough to bring the blood to a satisfactory level without grossly overloading the circulation.

Summary.

1. The pædiatric results of 71 pregnancies in Rh-negative mothers with antibodies are analysed.

2. Nineteen infants (26·7%) were unaffected, of whom five were Rh-negative, two Rh_0 (D) negative and 12 Rh_0 (D) positive.

3. Fifty-two infants were affected, of whom 10 were stillborn and 42 liveborn.

4. Of the 52 affected infants 19·2% showed congenital fœtal œdema, 69·2% showed *icterus gravis* and 9·6% anæmia without icterus, and the condition of one was indeterminate.

5. The prematurity incidence was greater than in the average population, and the incidence of prematurity ran parallel with the severity of the type of erythroblastosis.

6. The over-all fœtal wastage of affected infants was 27%—stillbirths 10, 19·2%; neo-natal deaths four, 7·7%. Of the four neo-natal deaths two were due to fœtal erythroblastosis, one was due to atelectasis and fœtal erythroblastosis, one was due to atelectasis—that is, straight-out uncomplicated fœtal erythroblastosis gave a neo-natal mortality of 3·8%.

7. The case histories of the four fatal neo-natal cases are given.

8. Thirty-six cases of *icterus gravis* with a mortality of 8·3% are analysed. The routine management of the cases is given.

9. The correlation of maternal blood and cord blood antibody titres with the condition of the infants is considered. While in general the more severe manifestations were associated with the higher titres, this did not apply in individual cases.

10. The history of previous erythroblastotic infants in the family is considered, and the mortality is considered from this standpoint.

11. The variations in the severity of the disease in successive pregnancies are emphasized. This aspect should be borne in mind when the worth of any therapeutic procedure is being evaluated.

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THE PROBLEM OF PELVIC PAIN.[1]

By F. A. MAGUIRE,
Sydney.

WHEN a patient complains of pain in the pelvis the real problem that faces the clinician is the interpretation of what that pain means. For pain is a signal, very often an important danger signal, that something is abnormal in one or more organs or tissues.

It is only in the last fifty years that real progress has been made in the study of pain. A summary of the modern views on the nature and meaning of pain should help us to arrive at a diagnosis in most cases.

Pain a Special Sense.

Pain is now accepted as a sixth and separate sense, quite apart from the so-called primary senses—sight, hearing, taste, smell and touch (Wolff and Wolf, 1948). It is served by its own special nerve endings. It has its own peripheral nerves. It travels by its own particular nerve tracts within the central nervous system, and has its own centres in the brain.

[1] Read at a meeting of the Section of Obstetrics and Gynæcology, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

Types of Pain.

Pain is usually classified as (i) surface or cutaneous pain and (ii) deep or visceral pain.

It is now accepted (Wolff and Wolf, 1948) that these may be divided into (*a*) bright, pricking pain, (*b*) burning pain and (*c*) deeper aching pain.

All of these may vary very widely in duration, in intensity, and in the rhythm of recurrence of the pain. Thus a pain may be mild, or short, sharp and severe. It may be continuous or intermittent. It may recur at regular intervals. Or it may have a special relation to a regularly recurring function, such as menstruation, micturition or defæcation. Again it may be brought on only by exercise, by coitus, or by other special causes.

Continuous severe pain has a very depressing effect on the nervous system.

Pain Nerve Endings.

Pain receptors are end organs separate and distinct from those for touch, pressure, heat and cold. They are naked nerve terminals which ramify amongst the cells of the tissues. They are scattered through the deeper layers of the skin and mucous membranes, the subcutaneous tissue, muscles, tendons and joints, and the viscera. They are specific for pain sensation.

The Nerve Fibres for Pain.

The nerve fibres which convey pain may be myelinated or non-myelinated, and are of various sizes. They travel either (*a*) directly to the posterior root ganglion in the somatic nerves, or (*b*) indirectly in the autonomic trunks and through the sympathetic ganglia to the posterior root ganglion by way of the white *rami communicantes*.

Gasser and Erlanger (1929, 1937) found that the anatomical classification as to size corresponded to the physiological classification as to function.

Class A fibres are large myelinated fibres ranging up to 20μ in diameter. They conduct impulses at speeds up to 100 metres a second.

Class B fibres are myelinated and smaller, ranging up to 3μ in diameter, and conduct impulses at speeds of three to fourteen metres a second.

Class C fibres are unmyelinated fibres. They conduct at a speed of less than two metres per second.

Thus pain may travel by a fast or a slow path.

Bright, prickling pain is carried by Class A fibres and travels fast.

Burning pain is carried by Class B fibres at a much slower rate.

Aching pain in muscles, bones and viscera travels mainly in sympathetic chains, presumably by both myelinated and non-myelinated fibres of varying sizes.

The Nerve Cells.

The cell bodies of all sensory nerves lie in the posterior root ganglion. The afferent splanchnic nerves pass through the sympathetic ganglion without interruption to reach their cell bodies in the posterior root ganglion.

The Relays in the Pain Path.

There are three relays of nerve fibres from the organs and viscera to the highest level in the brain.

First Relay.

Axons from the organs or tissues pass to the cells in the posterior root ganglion, from which a dendrite travels into the spinal cord, entering along the postero-lateral sulcus and ending around a cell in the grey matter of the posterior horn or column.

Second Relay.

The neuron from the posterior horn cell crosses through the anterior commissure to the opposite side of the spinal cord, and ascends in the lateral spino-thalamic tract to the lateral nucleus of the thalamus; but some fibres go by the spino-tectal tract to the roof nuclei of the mesencephalon.

Third Relay.

The neurons from the nerve cells in the thalamus form a third relay which goes by the thalamo-cortical radiation in the posterior limb of the internal capsule to the post-central gyrus of the cerebral cortex. However, pain may be consciously experienced (Johnston and Whillis, 1942) when the connexions existing between the thalamus and the cortex have been destroyed.

Cortical Connexions.

In the post-central gyrus of the cortex connexions are made with the highest integrative levels (Ray and Wolff, 1940) for the interpretation of the painful sensation; and these most likely determine the reaction of the individual to it.

As Wolff and Wolf (1948) put it:

> Appropriate noxious stimuli applied to any bodily structure equipped with pain endings may give rise to the sensation of pain. Whether or not pain occurs depends on the integrity of the pathways mentioned, the nature of the stimulus, its intensity and the individual's pain threshold.

Causes of Pain.

Pain may be caused in many ways. There is generally a local stimulus applied to the part or organ. Both surface pain and visceral pain may be caused by thermal, electrical, mechanical or chemical stimuli.

Pain in hollow viscera may be caused by excessive distension of the cavity causing stretching and tension in the wall, or by excessive muscle spasm or contraction causing colic. The pain in these instances is characteristic for the organ and can very often be localized to the organ by the individual by previous experience.

The Measurement of Pain.

Modern workers have recognized definite increments of pain, starting from the threshold of pain and working up to pain of maximum intensity. There are held to be 22 increments of pain. Every two such steps in the scale is now called a unit of pain, or a "dol" (Wolff and Wolf, 1948).

The Pain Threshold.

It is well known that people vary very much in their capacity to recognize pain. A stimulus that will cause much pain in one person may be barely recognized by another.

The level of recognition of pain is called the "threshold" of pain. It seems to be related to the natural make-up of the nervous system of the individual.

The pain threshold is probably about the same in all normal persons in good health. But it may be raised or lowered in any person by factors such as local injury or inflammation, by ill-health, by strong emotions such as exaltation, excitement, anger or fear, or by the use of drugs.

Hyperalgesia.

Local areas of skin may become more sensitive to pain than usual. Then a small local stimulus, such as a pinch or a prick, will cause much more pain than normal.

Lewis (1942) postulated a hypothetical "P" substance formed in the skin of the area involved, and also developed the concept of special "nocifensor" nerves as the ones subserving pain sensation.

However, Wolff and Wolf (1948) point out the following:

1. In some disturbances of the peripheral nerves—neuropathies—there may be an alteration of the effects on the "threshold" of the two types of cutaneous pain. Pricking pain travels fast, while burning pain is slow. The threshold for burning pain may be greatly lowered by the neuropathy, while that of pricking pain may be elevated. In the area supplied by the nerves affected, burning pain feels more severe, while pricking pain is less or absent.

2. Local inflammation with cutaneous hyperæmia will lower the strength of the stimulus required to produce local pain, which results in local hyperalgesia; for example, inflamed areas of skin or mucous membrane have a lowered pain threshold. An area of sunburned skin is much more sensitive to local stimuli than normal skin—that is, it is more "tender". The same condition is found in inflamed mucous membranes, such as those of the nasal mucosa, pharynx, larynx, trachea, œsophagus, stomach, bladder, rectum, vagina and vulva.

3. Where there is hyperalgesia in surface areas associated with pain "referred" from deep areas, the threshold for normal cutaneous pain is not altered, but the local hyperalgesia is due to noxious stimulation of the deep structures.

Reactions to Pain.

In general terms it may be stated that pain gives rise to definite reaction patterns. These may be for defence of the organ in general, or they may be certain feeling states (Wolff, 1943).

Cutaneous Pain.

Cutaneous pain seems to exert an exhilarating action and stimulates the subject to fight or flight.

Visceral Pain.

Visceral pain has a deeper aching quality and tends to exert a depressing effect. It is commonly associated with nausea followed by inactivity. This would seem to have a biological significance (Wolff and Wolf, 1948), since fight or flight would be fruitless against assaults from within. As Wolff and Wolf put it, "one cannot run away from an inflamed appendix".

Referred Pain.

Visceral or deep pains are dull and aching in quality and generally are poorly localized. They characteristically spread to be felt in areas other than those stimulated. The spread may involve deep or superficial pathways or both. This is "referred pain". It is thought to be due to the spread of the nervous impulse in the cord to other portions of the same segment, or to segments adjacent to those into which the noxious impulses are conducted. This gives rise to pain felt in parts innervated by deep and superficial branches of the affected segment. It also causes motor effects, such as skeletal muscle spasm, vasodilatation and sweating in the corresponding area of the body wall and surface.

Categories of Visceral or Deep Pain.

Wolff and Wolf (1948) classify deep or visceral pain into the following three groups.

1. *True Visceral and Deep Somatic Pain.*

True visceral and deep somatic pain is felt at the site of primary stimulation and may or may not be associated with referred pain. It is eliminated by infiltration of procaine into the site of noxious stimulation, or by blocking its afferent nerves; but it is not altered by infiltration of procaine into other structures supplied by the same or adjacent neural segments.

2. *Referred Pain.*

Referred pain may occur in addition to or in the absence of the true visceral and deep somatic pain just described. It is experienced at a site other than that of stimulation, but in tissues supplied by the same or adjacent neural segments. It may occur with or without associated hyperalgesia and hyperæsthesia.

Referred Pain without Superficial and/or Deep Hyperalgesia.—When pain occurs without superficial and/or deep hyperalgesia it depends only on the central effects of the spread of excitation of the original noxious impulses to the same and adjacent segments of the cord, whence they are relayed to higher centres for perception and interpretation. Injection of procaine into superficial or deep regions of referred pain does not reduce the intensity of pain due to this mechanism.

Referred Pain with Superficial and/or Deep Hyperalgesia.—Referred pain may be accentuated in intensity by virtue of the effects of ordinarily non-noxious stimuli from zones of reference. Impulses from such sources, normally inadequate to produce pain, may do so upon reaching the cord in a segment involved in the central spread of excitation. Procaine injected into superficial or deep hyperalgesic structures will cause abolition of this element of the referred pain phenomenon, resulting in more or less reduction of the subject's discomfort, depending on the amount of hyperalgesia.

3. *Pains due to Secondary Skeletal Muscular Contractions which provide a Fresh Source of Noxious Stimuli.*

Pain may result from the secondary effects of the central spread of excitation on the effective structures, including painful contractions of skeletal muscles. Such disturbances may be widespread, and pains may be felt in situations remote from the original source of noxious stimuli. Local infiltration of the contracted muscles with procaine abolishes this type of pain by disrupting its peripheral mechanism.

It is suggested also:

1. That segmental phenomena within the spinal cord and brain stem account for the spread of the afferent and efferent effects associated with deep noxious impulses and pain.

2. That localization involves conditioning, familiarity or previous experience, and therefore cerebral or cortical function.

3. That "hyperæsthesia" and hyperalgesia associated with deep pain result from normal threshold impulses, and that as a result of modification within the central nervous system they are interpreted as more intense and of longer duration.

The Pain Pathways from the Pelvic Organs.

The Vulva.

The somatic nerves involved in pain pathways from the vulva are the second, third and fourth sacral via the internal pudendal nerve, and the first and second lumbar via the genito-femoral nerve in the *mons pubis* and anterior part of the vulva.

The splanchnic nerves involved are the second, third and fourth sacral via the parasympathetic "*nervi erigentes*".

Area of Referred Pain from Vulva.—The area of referred pain from the vulva is made up of (*a*) the sacral area of the back, (*b*) the buttocks and perineum, (*c*) the back of the thighs and legs as far as the heel, and (*d*) occasionally, from the anterior part of the vulva, the groins (first and second lumbar).

The Vagina.

The nerves involved in pain pathways from the vagina are the same as for the vulva, less the first and second lumbar.

The Uterus and Uterine Tubes.

For the uterus and uterine tubes splanchnic nerves only are involved. There is a double innervation as follows.

The Cervix and Lower Uterine Segment.—From the cervix and lower uterine segment pain impulses travel by the second, third and fourth sacral nerves via the "*nervi erigentes*", entering the lowest segments of the spinal cord. The area of referred pain consists of (*a*) the sacral area of the back, (*b*) the buttocks, and (*c*) the back of the thighs and legs as far as the heel.

The Body of the Uterus and Uterine Tubes.—From the body of the uterus and uterine tubes sympathetic afferent fibres pass through the superior hypogastric plexus to the tenth, eleventh and twelfth thoracic and first lumbar segment of the spinal cord and by the ovarian leash also. The area of referred pain consists of the lower part of the

abdominal wall from below the umbilicus to the groins, the "tubo-ovarian triangle" on each side.

Note: There is also a parasympathetic path by the ovarian leashes to the aortico-renal and cœliac ganglia by fibres of the vagus nerve, going by the vagus afferent splanchnic fibres to the chief dorsal nucleus of the vagus in the lower part of the brain stem—the medulla in the lower part of the floor of the fourth ventricle.

The Ovary.

Splanchnic innervation from the ovaries is by the sympathetic fibres in the ovarian leash to the tenth thoracic segment of the cord, the ovary developing originally at this level. The area of referred pain is the anterior abdominal wall opposite and just below the umbilicus.

The Bladder.

The bladder has the following double (splanchnic) innervation: (*a*) from the region of the trigone and urethra by the second, third and fourth sacral nerves to the lower part of the spinal cord; (*b*) from the fundus by the sympathetic afferent fibres via the superior hypogastric nerves to the twelfth thoracic and first lumbar segments.

Area of Referred Pain.—The area of referred pain from the trigone and urethra is (*a*) to the lower sacral area of the back, (*b*) to the buttocks and perineum, and (*c*) down the back of the thigh and leg to the heel. From the fundus it is to the lower part of the anterior abdominal wall above the pubes and the groins.

It has been shown (McLennan and Goodell, 1943) that the mucosa lining the urethra, bladder, ureters and kidney pelvis is sensitive to pain.

Rectum.

Through splanchnic innervation, pain from the rectum travels by the second, third and fourth sacral nerves to the sacral segments of the spinal cord.

Area of Referred Pain.—The area of referred pain is the lower sacral area, the buttocks and the back of the thighs and legs.

The sensory functions of the sympathetic and parasympathetic nerves are different.

Theodore C. Ruch (1947) has pointed out that sensory impulses underlying organic sensation are conducted to the central nervous system entirely by way of the parasympathetic system. For example, if the sympathetic nerve supply to the stomach is severed to relieve pain, it does not stop the feeling of hunger due to hunger contractions. But in the sacral division, sensations of bladder fullness are completely ended with blockage of the pelvic nerve (parasympathetic) or its roots, the "*nervi erigentes*".

The Peritoneum.

The visceral peritoneum is insensitive to local stimuli such as pricking, cutting or pinching. But any pull on a mesentery attaching a viscus to the abdominal wall causes pain. However, recent work (Wolff and Wolf, 1943) has shown that under appropriate stimuli both the mucosa and the deeper structures of the gut are sensitive to pain.

The larger arteries of the mesenteries and the parietal peritoneum are sensitive to pain. A pull from traction will cause pain, due probably to pull on the arteries.

The parietal peritoneum is said to be very sensitive. But it is not settled yet whether this is a quality of the inner smooth surface of the peritoneum or of the subserous connective tissue. Conflicting views have been put forward; Morley (1931) claims that the peritoneum itself is very sensitive to direct stimulus, while Capps and Coleman (1922) have explored the inner surface with a bent wire through a cannula and found it insensitive. However, there is no doubt that the subserous tissue lying against the peritoneum is acutely sensitive. It draws its nerve supply from the adjacent somatic nerves, and its pain impulses would travel by them to the spinal cord.

When the parietal peritoneum is inflamed or irritated, these nerves carry the pain to the spinal cord and cause the referred pain and muscle spasm that occurs in the anterior abdominal wall in acute peritonitis.

The Pelvic Connective Tissue.

The pelvic viscera are closely surrounded by much loose connective tissue, which in pathological states is soon involved—for example, in inflammation or malignant disease of the organs. It is rich in sympathetic nerve fibres and also has some somatic nerve fibres from the internal pudendal nerve (second, third and fourth sacral). Any irritating condition of the pelvic connective tissue causes the deep dull ache of visceral pain.

The Special Sensations of Pelvic Organs.

The rectum and bladder have their own sensations. These if within physiological limits are not painful. The sensation of fullness gives rise to the desire for micturition or defæcation. But if the organ is over-full or forcibly distended, pain is felt. This may become acute and intolerable. Similarly spasm of the wall of the rectum or bladder may cause intense pain and strangury.

The normal uterus, tubes and ovaries are sensitive to touch. A normal vaginal exploration causes discomfort if pressure is made on a normal uterus or on the ovary. The ovary has its own characteristic sensation of a "sickening" feeling if squeezed between the examining fingers. It is said to resemble the pain felt in the testis when that organ is squeezed.

But in pathological conditions, particularly of inflammation, these organs may become acutely tender to palpation. In these conditions a thorough bimanual exploration of the pelvis, if carried out very gently and with the cooperation of the patient by adequate relaxation, can give most valuable information to the doctor. If a patient has a pelvic pain, and if on gentle and thorough exploration one can reproduce that pain by localizing and squeezing or drawing on one particular organ, such as the uterus, a tube or an ovary, one has gone a long way towards establishing a diagnosis.

I have found it a great help in exploring the pelvis to use what I call the three-position examination. This is carried out as follows:

1. Make an examination with the patient in the ordinary dorsal position, when the uterus can be located and the pelvis generally explored.

2. With the examining fingers still in position, ask the patient to put both legs straight out on the table. The abdominal wall can be relaxed by the patient still more than in the first position by her taking deep breaths with the mouth open. The lumbar curve is tilted forward. The pubis is lowered, the sacrum is raised, and the uterus, tubes and ovaries come much closer to the anterior abdominal wall and can be outlined and identified with greater ease and certainty.

3. Ask the patient to resume the dorsal position, and while gently lifting the pubic arch with the examining fingers still in position, ask the patient to "lift her tail off the table". She then bends from the waist lifting the pelvis clear of the table. By turning the examining hand with the palm down, one can outline all the structures on the posterior pelvic wall and identify the sacrum, the great sciatic notch with the pyriformis and the great sacral nerve trunks, and the sacro-spinous ligaments, and can explore the front and sides of the rectum. By going to one or other side of the pelvis, one can locate the spine of the ischium and from it can place the internal iliac vessels, the ureter and the glands on the side wall of the pelvis. One can also, by putting the other hand under the buttocks, carry out a bimanual examination of the structures in the great sciatic foramen, the lesser sciatic foramen and the ischio-rectal fossa.

I would advise you to try this method on an articulated pelvis to get the exact location of the bony parts, and you can then place the position of the soft parts in relation to the bones.

If this method is used, slowly and patiently, one can, with a great deal of confidence, place the location of many inflammatory conditions and newgrowths in the pelvic cavity.

It is essential in all cases of pelvic pain to take a careful and detailed history, with special reference to the time and manner of the start of the pain, how it has progressed, and particularly any regular recurrences or the relation to normal physiological cycles of menstruation, defæcation, micturition and, if necessary, coitus. This history, viewed in the light of what may be found on pelvic exploration and the study of any referred pains or sensitive areas, should enable one to arrive at a reasonably certain diagnosis as to the cause and location of the pathological lesion or the diseased organ or organs.

The Treatment of Pain.

The best treatment of pain is to find the cause and remove it. This does not necessarily mean surgical intervention. The gynæcologist should be a physician first, and try to relieve the patient by medical treatment unless the condition is an acute surgical condition demanding immediate operation. If one can relieve the pain and give the patient peace and comfort, many pathological conditions can be made to settle down, and often be cured, by modern medical methods of treatment. But pain is exhausting and demands relief.

The Relief of Pain.

There are many drugs that will raise the threshold of pain and so give relief and rest.

Morphine and its derivatives, heroin, codein, pethidine *et cetera*, are the most potent drugs for raising the threshold of pain and relieving pain. But they must be used with judgement and discretion. Their disadvantages are well known.

There are several groups of drugs that act as analgesics. It is found, however, that when two different drugs act in this way they do not reinforce each other or add together in the summation of their effect on raising the pain threshold. The stronger drug has its own effect to its normal level and the weaker one has no effect. Furthermore, each drug has an optimum dose for relieving pain, and an increase in this does not relieve pain more than the optimum dose.

Acetylsalicylic acid, acetanilid, phenacetin and amidopyrin act primarily on the threshold of pain. Repeated doses of the one drug, used so as to keep the threshold high, are found (Wolff and Wolf, 1948) to provide the most effective way of dealing with pain as far as perception is concerned. Wolff and Wolf found, for instance, that repeated doses of three grains of acetylsalicylic acid at two-hourly intervals maintained the pain threshold steadily at a high level.

There are many new analgesic drugs put forward by the manufacturing chemists. These must all be assessed by their effect on the pain threshold.

The Surgical Relief of Pelvic Pain.

The surgical removal of pathological conditions will relieve pelvic pain. But the surgeon must satisfy himself that the operation he intends to perform is dealing with the real cause of the pain. To correct a retroversion surgically in order to cure a backache, when the cause of the backache is a damaged sacro-iliac joint, is futile and may do the patient psychological harm.

In many painful conditions of spasmodic dysmenorrhœa pre-sacral neurectomy will give relief after other methods have failed. But the surgeon must be sure (Meigs, 1939) that he removes all the nerve tissue between the two common iliac arteries down to the top of the sacrum. The operation requires good exposure. The dangers are the left common iliac vein, the two ureters and the middle sacral artery. Careful choice must be made of the patients for this operation. All pelvic pathological conditions should be attended to as well. It will not relieve backache. Backache is not controlled by this plexus. Pregnancy is not interfered with. Bowel and bladder habits undergo no serious change.

In malignant disease of the viscera the growth often extends into the spinal nerves, causing pain by the somatic path. In these conditions the pain cannot be relieved by pre-sacral neurectomy. Section of the posterior nerve roots or anterior cordotomy may be required in these cases. But great relief can be given in intractable pelvic pain by injecting alcohol into the lower spinal canal. This needs to be done by one well-skilled in the technique of spinal injections.

Anterior cordotomy gives consistent and satisfactory relief from pain. It will not interrupt the sensation of a distended œsophagus, colon or bladder (Association for Research in Nervous and Mental Disease, 1943).

Psychosomatic Pain.

It does not always follow that because a patient complains of pain she has pain. Patients may use pain as a defence mechanism, to avoid unpleasant tasks or appointments, or because of an inferiority complex.

If this is suspected, watch the patient carefully and look for confirmation of her statements. See how she reacts to examination. Agony may be assumed. Look for other signs, such as raised pulse rate, sweating, pallor, dilated pupils. If in doubt, distract the patient's attention by conversation, other manipulations and so on, and see if the evidence fits in with the patient's complaint.

Finally, approach every case of pelvic pain as a real problem to be solved. The application of anatomical and physiological principles combined with careful, patient and accurate history-taking and a thorough gentle examination, and coupled with clinical acumen and mature judgement, should enable the doctor to solve most of these problems and give his patient relief and health.

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MEDICAL ASPECTS OF PERIPHERAL VASCULAR DISEASE.[1]

By KEMPSON MADDOX,
Sydney.

THE traditional classification of peripheral vascular disease (which I have interpreted for present purposes as organic occlusive arterial disease) has been into obliterative arteriosclerosis of the senile type, *thromboangiitis obliterans*, simple arterial thrombosis, specific arteritis, and *periarteritis nodosa*, together with the results of trauma, embolism and physical agents such as cold. More recently the Manchester group, mainly as a result of arteriographic study, have suggested that obliterative arteritis of the lower limbs should be divided into three classes, namely, primary thrombosis of the popliteal artery, juvenile obliterative arteritis (Buerger's disease) and senile obliterative arteritis. They state that the first two classes can be separated from the last at the age of thirty-five years. Primary popliteal thrombosis appears to be a localized angiographic and pathological entity, probably of traumatic origin, and with a good prognosis. Juvenile obliterative arteritis begins in the feet and ascends in the limb, preceded by venous thrombosis. The legs are affected unequally. It is the main contributor to the well-known Buerger's syndrome. One limb has usually been lost within five years of the onset.

Senile obliterative arteritis includes the greatest number of patients, and itself consists of three subgroups, namely, diffuse obliterative arteritis, secondary popliteal thrombosis and secondary femoral thrombosis, occurring in this order of frequency and readily discerned by arteriography. The site of the arterial block and the degree of development of the collateral circulation at the time of occurrence of the thrombosis determine the clinical findings. The symptoms and signs of the ischæmic limb are known to you all.

I propose to confine my remarks to a broad consideration of the commonest type, that is, senile and presenile arterial disease of the extremities (*arteriosclerosis obliterans*), of which I have seen a great deal in sixteen years' work in a large diabetic clinic. We cannot halt the progress of arteriosclerosis, even in diabetics who are seemingly well stabilized; nor can we influence, with any confidence, the inexorable spread of that dreadful affliction *thromboangiitis obliterans*, which some maintain is really a more acute presenile form of obliterative arteriosclerosis. Arterial disease is increasing in frequency because of the advancing age of the general population. But there is a strong suspicion that arteriosclerosis of coronary and other arteries is increasing in individuals under the age of thirty-five years. Arteriography has demonstrated the frequency of occult thromboses in the peripheral arterial tree, which have occurred quite unnoticed or have been distinguished as "neuritis" or "sciatica" or as a more severe or prolonged episode of intermittent claudication. Such a development may have been the sequel to severe exercise or to some minor local infection or trauma. In this way a close analogy exists between coronary arteries and those supplying peripheral skeletal muscle. In each, gradual unobtrusive closure can occur, or a dramatic and violent crisis of pain can indicate sudden block of a major channel. In each the pathogenesis of pain is probably identical, as a result of the accumulation of Lewis's P factor about the afferent nerve endings. The pain felt is referred to the appropriate sclerotome, and is accompanied by local tenderness and certain reflex phenomena, such as vascular spasm in the same segmental area and, if continued, even certain trophic sequelæ. The pain on exercise disappears only when the collateral supply becomes adequate or when the ischæmic muscle becomes completely fibrotic. Apart from its remarkable specificity, the diagnosis of intermittent claudication from other forms of referred pain is readily proven by the injection of a little local anæsthetic agent into the area of muscle tenderness, after which the subject can walk a surprisingly long distance without discomfort. It must further be remembered that the arterial obstruction may exist high in the femoral artery or even more proximally. The physician's contribution is mainly directed towards control of factors considered to be capable of initiating or fostering arterial degeneration, towards anticipation and recognition of its development, and towards educating the already affected patient to avoid practices which commonly give birth to gangrene.

The influences which predispose to, and accelerate, peripheral arteriosclerosis are not all understood. The influence of heredity is less a matter of genetic proof than one of clinical experience. Heredity is often extraordinarily selective for cerebral or coronary artery degeneration, but its role is less specific in the case of the limb arteries. Racial influences may be more related to the quantity and quality of national dietaries. Arterial hypertension is commonly accepted as an accelerating influence, and the higher average pressure in the lower limbs tempts one to offer this as an explanation for the fact that the feet are the chief victims of *arteriosclerosis obliterans*. The role of high blood pressure is less definite in the older patient with "quiet" vascular insufficiency of the feet and visible calcification of the arteries. A diabetic factor is detectable with surprising frequency if the examiner performs a glucose tolerance test rather than a simple urine test for sugar. Smoking and anxiety are probably only aggravating vasoconstrictor influences, not playing any true ætiological role. Metabolic disturbances, as a result either of high lipoid content in the diet or of endocrine influences, have been under review recently, but investigations are hampered by our ignorance of the intimate processes of lipoid metabolism. Perhaps one day it will be shown that the high cholesterol diet of the whole Occident will have to be radically modified. Is it that the leg and foot vessels are more susceptible because of the transfer of cholesterol from a sluggish blood-stream to the intima? Are our sedentary customs conducive to an increase of peripheral vascular disease? Has the indubitable increase in our midst of hypertension and diabetes contributed materially? These questions await an answer.

In an assessment of any patient with peripheral vascular insufficiency we must try to determine the extent of past arterial damage and present function. The latter depends on the degree of narrowing *plus* added vasoconstriction. Most of the best tests for peripheral circulation can be performed only in the laboratory. Techniques which provide objective evidence include "whole limb" plethysmography, performed at a constant room temperature and at a suitable interval after smoking or feeding, both before and after full vasodilatation has been effected. Such equipment must be available in a large hospital when surgery is contemplated. The oscillometer gives little more information than can be achieved by visual and tactile examination. The thermocouple is only slightly more sensitive than the trained hand, and records the skin temperature only. The intradermal and histamine tests are open to the same objection. Instruments measuring only the toe or finger circulation are of limited clinical value because the important arterio-venous shunts in the sole and palm are neglected. What is needed, if amputation is contemplated, is a cross-sectional assessment of blood-flow. The injection of radio-sodium, with the timing of its arrival at various levels by the Geiger counter, is recommended by those who have access to such tools, as a reliable method of obtaining this type of information.

When the distribution of arterial blood has been revealed by such procedures, an estimate of functional arterial capacity becomes essential in respect of treatment and prognosis. Such information is available only on repetition of the above-mentioned tests after maximal vasodilatation has been attained, either by heating the remainder of the body or by paralysing all vasoconstrictor influences by means of spinal anæsthesia, lumbar sympathetic block or peripheral nerve block. Psychogenic vasospastic influences are probably less operative in senior decades, but smoking is common and should be prohibited for two hours before a test. I believe that, therefore, for everyday clinical

[1] Read at a combined meeting of the Section of Medicine and Section of Surgery, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

purposes the only items of equipment necessary for testing the peripheral arteries are a warm room, a trained eye and a trained hand, and some blankets and hot-water bottles. Objective methods have their place in recording serial changes in foot circulation, and for the information of a subsequent observer the special apparatus required should be available in large hospitals and special vascular clinics.

At the first objective sign of organic vascular disease the patient should be so informed, and his education should begin in the methods of encouragement of a collateral blood supply and in the care of the skin of the feet. Smoking and "Benzedrine" should be strictly forbidden and alcohol mildly encouraged. He should adopt a diet of high protein, low cholesterol content. If he is obese, calorie intake should be controlled drastically. He should practise a daily ceremonial of Buerger's exercises and walk gradually increasing distances at a pace just below the claudication point. He should try hard to solve existing psychological conflicts and problems, if necessary with the aid of skilled advice and simple sedatives, and avoid the assumption of fresh responsibilities which may be the origin of future anxieties. Cold is to be shunned, and high altitudes, sea bathing *et cetera* are undesirable, while his personal clothing should be warmer than before. Such measures will encourage peripheral vasodilatation in general. We cannot selectively bring about an increase in the number and size of collateral vessels, but possibly we can offer some encouragement by gently increasing tissue demands for oxygen, which the main vessels are no longer capable of fulfilling. The rules for foot hygiene are well known to you all, but an explanation of the modes of the origin of gangrene, intractable paronychia or ulcer is of vital importance in the educational programme for the victim of ischæmic feet. These are blisters from ill-fitting footwear, accidental trauma, such as carelessness in stubbing a toe or dropping a heavy object upon it, infection from dirty nail scissors, pressure on the popliteal space of the calf, interdigital cracks due to mycosis, application of caustic antiseptics, sunburn and corn or callus paring. Other precipitating factors, such as increased blood coagulability, either spontaneous or following systemic infection, are less understood and cannot be avoided by the patient, but the urgency for skilled medical attention after sudden pain in the limb, denoting arterial thrombosis, should be impressed upon him.

In prognosis the rate of progress of the vascular insufficiency is more important than the degree reached. In the absence of infection many very ischæmic limbs, if treated with respect and intelligence, will remain seemingly static for long periods of time, even up to five years at least, in this country. Others show steady deterioration in spite of all conservative efforts. Many patients have to continue work of a type which increases the risk of minor trauma or over-exertion, or are subject to our common frailties of carelessness and lack of purpose. In others, pain becomes unbearable, or the appearance of gangrene quickly modifies our conception of treatment and prognosis. In the end, all our prophylaxis and treatment does little more than preserve the foot for a few more years at the most, and often for less.

For many years the physician has done his best with vasodilator drugs, the efficacy of which has been negligible because of the weak or transient character of their effects on peripheral arterial blood-flow. It has been difficult, too, to measure objectively their results, because reliable measuring equipment, such as the thermostromuhr, which has proved so valuable in the animal laboratory, has not been applicable to man. Let us frankly admit that the administration of acetyl choline and its derivatives, typhoid vaccine, hypertonic saline by intravenous injection, testosterone and tocopherols belongs to the domain of wishful thinking and wastes precious time. I personally have had little success with tissue extracts, such as "Padutin" (a protein-free extract of the pancreas), or from intermittent venous occlusion. Recently important substances have become available which specifically reproduce the effects of denervation of the limb. The first group of these contains the tetraethyl ammonium ion, for example, tetraethyl ammonium bromide, which will perform a momentary "chemical sympathectomy" by adrenergic blockade (dibenzylbetachloroethylamine hydrochloride), and "Priscol" (2-benzyl,4-5imidazoline hydrochloride); all of this group produce peripheral vasodilatation, but have unpleasant side effects, and their action is too transitory for therapeutic use. Recently Mufson, at the New York Hospital, has claimed that remarkably long periods of vasodilatation in ischæmic limbs followed the administration of one milligramme of histamine base in 500 millilitres of saline from a pressure bottle directly into the femoral artery. His experiences await confirmation. The one medical measure which can be depended upon in the presence of ulceration or pain is rest for the limb and for the patient. The result of conservative hospital care with control of infection and hyperglycæmia, procurement of sleep, good food and sustained recumbency *plus* the effects of suggestion can be astonishingly good and has placed some difficulties in the way of true assessment of drug therapy.

Sympathectomy involving the removal of the first three lumbar ganglia and the intervening chain has given us a definitive means of releasing vasomotor tone in all superficial vessels at least, good and bad, in the lower limbs, even though the vessels are subsequently three times more susceptible to the effects of adrenaline. The effects of pre-ganglionic sympathectomy persist for a long time, give relief from "rest" pain (not from claudication), allow ulcers to heal and delay the onset of gangrene. Sympathectomy should be performed only on patients who are less than sixty years of age, without hypertension, on those who have a good vasomotor response, and on those with no evidence of coronary artery disease, hypertension or extensive gangrene. Calcification of main vessels does not always mean an unsuccessful result. If the general condition of the patient is unsatisfactory, the upper lumbar ganglia can be destroyed by injections of 10% phenol solution.

I trust that the physician of the future will invite the aid of the neurosurgeon long before the patient becomes bedridden, and at a phase when the vital collateral circulation has not itself become blighted. It is not uncommon to see the operation postponed until the patient is so worn out and wasted by pain, loss of sleep, nutritional deficiency, protein loss and bacterial toxæmia that the healing properties of his tissues are seriously impaired. Correction of these factors is as important after operation as before. Penicillin has altered the outlook considerably, especially in diabetic gangrene. It must be given in doses three or four times those usually employed, because of impaired diffusion into the line of demarcation, and preferably the first dose should be injected directly into the femoral artery.

Similarly, there is a strong case for continued treatment with dicoumarol in the presence of gangrene or infection, pending the surgical intervention. The physician is interested in these preamputation questions, also in the risks of the operation, in types of anæsthesia and in the important problem of rehabilitation and after-care. Mr. E. J. Hallstrom, of Sydney, has prepared a limb refrigerator which permits the operator to vary the rate and depth of cooling at will. We have not had any personal experience with this equipment, but we have used the actual ice-pack six times. The rapid relief of pain and toxæmia in a patient with extensive gangrene is most gratifying, and the surgical anæsthesia often complete. We must respect, however, the damaging potential of cold, if continued for long, and the final place of this technique is not yet determined. The reluctance on the part of most patients to wear a prosthesis after supracondylar amputations and the advent of the antibiotics and anticoagulants have resulted in a trend towards conservatism, which is justifying itself, at least in the hands of McKittrick, with his transmetatarsal amputation and the knee-saving operation of B. C. Smith. Further, Boyd has shown the value of tenotomy of the *tendo Achillis* when claudication has produced complete crippling.

In the end, the question of treatment resolves itself into the question of increasing blood supply to meet the demand, or reducing the demand to meet the supply (by neurectomy or tenotomy). Each case must be considered as an individual problem, and regard paid to ætiology, age, general physical condition, economic status and occupation, the influence of suggestion in treatment, the severity of symptoms, the distribution of vascular disease in the limb, skin *versus* muscle ischæmia, and the risk to life *versus* the risk of losing the limb.

ISOLATION OF A VIRUS FROM ENCEPHALITIS IN SOUTH AUSTRALIA: A PRELIMINARY REPORT.

By J. A. R. MILES, M.A., M.D., B.Chir., M. C. FOWLER, M.D., B.S., and D. W. HOWES, B.Sc.,
From The Institute of Medical and Veterinary Science, Adelaide.

A GIRL, aged ten years, from a country district 75 miles north of Adelaide, developed encephalitis, rapidly went into coma and died on February 22, 1951. An autopsy was carried out the next day. Through the kindness of Professor J. B. Cleland we received the brain of this patient.

Histological Examination.

Paraffin blocks were made of pieces of tissue selected from the cerebral cortex, thalamus, mid-brain, medulla and cerebellum. Sections were stained with hæmatoxylin and eosin and with Weil's myelin sheath stain.

Lesions were found in the grey matter of all these structures. The spinal cord was not available for examination.

Macroscopic examination of sections stained by Weil's method revealed tiny round pale areas measuring up to a millimetre in diameter, particularly in the cerebral cortex and thalamus. The lesions in the latter were coalescent. In these foci, which were on the whole well defined, recognizable nerve cells had, for the most part, completely disappeared, the glial nuclei were pyknotic, and the ground substance was converted into a spongy network of tiny spaces by œdema fluid. Dilated capillaries ran through the lesion, hyperæmia being invariable in affected areas. Parenchymatous reaction to the damage was scanty, consisting of occasional microglia in the *"Gitterzell"* stage; perivascular cuffing with lymphocytes was infrequent and slight. Necrotic neurons were shrivelled, commonly exhibiting eosinophilia, and contained a densely staining distorted nucleus. The dead cells were often, however, represented only by an ill-defined area of eosinophilic staining overlaid with microglia, whose nuclei were often themselves in various stages of pyknosis and karyorrhexis. No inclusion bodies were demonstrable in any cells in or around these foci.

In the cerebellum the Purkinje cells were selectively attacked in a patchy fashion; while lesions were scattered throughout the medulla, the reticular formation and the inferior olivary nuclei were most severely involved. Although acute changes similar to those in the thalamus and cerebral cortex were to be found, many of the cells in the medulla and cerebellum were undergoing degeneration with no more surrounding disturbance than a mild microglial proliferation.

Severe changes, of the acute œdematous character, were present in the red nucleus and *substantia nigra*; in the latter, phagocytosis of melanin particles was a striking feature.

Experimental.

A pool of material from all parts of the brain was extracted in 10% serum saline solution and, after addition of 500 units of penicillin and streptomycin per millilitre, was inoculated intracerebrally to suckling and weaned mice, guinea-pigs and rabbits.

The guinea-pigs merely showed a rise in temperature above 104° F. on the fifth day and the rabbits no abnormality, but five of six suckling mice inoculated died between the third and eighth days after inoculation, and four of six weaned mice died on the sixth day. Passage from suckling mice led to the death of all suckling mice on the fourth day and of weaned mice on the fourth or fifth day. The agent passed readily through a 600mμ gradocol membrane and was unaffected by 500 units of penicillin and streptomycin per millilitre. Up to the sixth passage weaned mice inoculated intracerebrally with large doses of virus have died on the fourth or fifth day after inoculation.

The LD50 of the virus for weaned mice by intracerebral inoculation of fourth passage material was 0·03 millilitre of a 10^{-7} dilution. A 5% suspension of the same material showed virus activity after passage through a 100mμ average pore diameter gradocol membrane, but not after passage through a 60mμ average pore diameter membrane.

The fourth passage mouse material was inoculated by the intracerebral route into two young rhesus monkeys. These began to show symptoms on the sixth and eighth days after inoculation. At first they showed tremors only, then convulsions and gross ataxia, followed by great weakness, without complete paralysis of any limb, although one has shown almost complete ptosis of one eyelid. The first became moribund in forty-eight hours and was killed. The second has shown less severe disease and may recover.

In further guinea-pigs evidence of persistence of the virus up to at least the sixth day was obtained. Rats aged twenty-eight days have proved non-susceptible.

Embryonated hen's eggs incubated from five to eight days before inoculation into the yolk sac of generous doses of virus have died between forty and seventy-two hours after inoculation. The beheaded embryos and yolk sacs from such eggs have been used as antigens for a complement-fixation test.

The 20% saline suspensions were extracted overnight at +2° C. and the yolk sac antigen was treated with ether in the cold. Both antigens had large particles removed by centrifugation and they were then used without further purification. The yolk sac antigen proved completely inactive, but the embryo antigen yielded positive complement-fixation findings with sera from those animals (rabbits, guinea-pigs and rats) which had not developed clinical disease after intracerebral inoculation of the virus. These sera did not yield fixation with an antigen made from normal chick embryo tissues.

Examination of sera from five human contacts of the infected patient, including three children who had had sore throats recently, showed no complement-fixing antibodies against the active antigen. Sera have also been tested from patients in two non-fatal cases of encephalitis at present in hospital in Adelaide. One of these taken three weeks after the onset of the disease yielded negative results. The other, taken two months after the onset of the disease, gave complement fixation with our test antigen to the high titre of 1:80, but none with the control antigen.

Shortly after the death of our patient a horse died after a very acute illness only a short distance away. Unfortunately we did not hear of this death until a fortnight after its occurrence. Two other horses, reputed to have shown minor ill health, were bled and their sera tested, but no complement fixation greater with the test than with the control antigen was demonstrated.

These tests are being checked by neutralization tests, which are still in progress, but it is safe to say that they substantially confirm the findings of the complement-fixation test.

Conclusion.

A virus has been isolated from a fatal case of acute encephalitis in South Australia. There were no other clinical cases of encephalitis in the district, and we have not obtained any serological evidence of other infections in the immediate neighbourhood, but in one of two non-fatal cases of encephalitis the patient, who is in hospital in Adelaide, is carrying antibodies to our agent.

A single filtration experiment suggests that the size of this virus is of the same order as that of the arthropod-borne viral encephalitides.

Our case differs from the classical picture of X disease (Cleland and Campbell, 1919) in the lack of cellular infiltration in the brain; but this may be within the limits of individual variation, and the clinical picture in the monkey is exactly like that of X disease.

The picture in both experimental animals and eggs is quite different from that in louping ill, of which one of us had had considerable experience. It is, however, very similar to that of Japanese B encephalitis, except for the failure in early passage to cause disease in rabbits (Kasahara *et alii*, 1936; Webster, 1938; Koprowski and Cox, 1946).

Acknowledgement.

We wish to thank Dr. G. H. McQueen for his help in collecting the blood specimens and the Superintendent of the Adelaide Children's Hospital for his cooperation.

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Reports of Cases.

A CASE OF BUPHTHALMOS TREATED BY GONIOTOMY.

By M. C. MOORE,
Adelaide.

IN 1947 Barkan reported the results of his treatment of buphthalmos by the operation known as "goniotomy" with success in a much higher percentage of cases than the drainage operations commonly used have given. The technique of goniotomy consists of passing Barkan's knife-needle through the cornea at the limbus and carrying it across the anterior chamber into the angle at the opposite side, where the angle is incised throughout an area of about one-quarter of the circumference of the cornea. This clears a passage through the embryonic remains blocking the angle and opens a passage for drainage of the aqueous into the trabeculæ.

The following is the report of a case treated in this way.

Baby L.B. was examined first at the age of four months. His mother gave the history that she had noticed the cloudy appearance of the cornea of each eye first when the child was three days old. She had been operated on for ovarian cyst on four different occasions, only a small part of one ovary remaining after the last operation. Later, when she underwent a further operation for "fibroid", she was found to be five months pregnant. A Hogben test had been carried out twice at the fourth and fifth months of her pregnancy. There was no history of other illness during her pregnancy, nor was there a family history of buphthalmos.

Both of the child's corneæ were large and very steamy, although no tears in Descemet's membrane could be seen. The pupils reacted, were round and quite small. The tension was high.

On July 12, 1950, with the child under deep ether anæsthesia, the tension of the right eye was 35 millimetres of mercury (Schiotz) and that of the left 40 millimetres. Corneal diameters were 13 and 14 millimetres respectively. Owing to the steaminess of the cornea, the fundi could not be seen. Goniotomy was performed on both eyes as described above.

There was slight bleeding into the anterior chamber in each eye, which stopped immediately. The blood cleared over the next two or three days, and eserine was used to keep the pupils small for two months. The cornea of each eye cleared considerably at the time of operation, and the improvement continued for two to three weeks afterwards.

On August 2, 1950, with the child under anæsthesia, tension in the right eye was 27 millimetres of mercury and in the left 32 millimetres, but eserine was still being used. This was stopped on September 6, 1950.

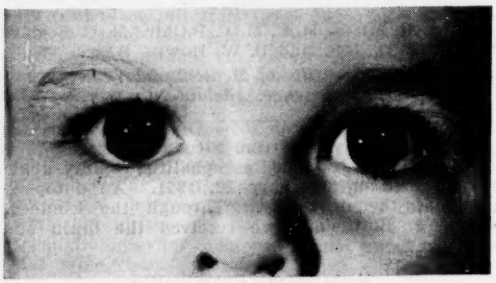

FIGURE I.
Baby L.B., four months after goniotomy.

The left cornea has remained quite clear since then, and its tension has stabilized at about 20 millimetres of mercury. However, it was necessary to repeat the procedure twice on the right eye before the tension became stable at about this same value. On the last occasion the tip of the knife was carried through at the end of the incision to emerge under the conjunctiva—"goniopuncture", described by Scheie (1950). A different region of the angle was used. Eserine has not been used for three months, and the tension has remained stable within normal limits in both eyes. Although the left cornea appears normal, the right has a slight but generalized milkiness throughout the *substantia propria* which seems to be stationary. The difference between the two corneæ can be seen in the photograph. The small area of pigment visible at the limbus may be avoided by introducing the knife well in front of the limbus. The right eye is myopic and had slight cupping of the optic disk. The left eye has a moderate degree of mixed astigmatism, and its optic disk is normal.

It is interesting to note that the improvement in tension and in the appearance of the cornea seems to continue for two or three weeks after the operation.

The mother of this child underwent an abdominal operation at her fifth month of pregnancy. Hogben tests were also performed at the fourth and fifth months. At this time in the development of the fœtus the angle of the anterior chamber is occupied by tissue which usually disappears to allow drainage at the angle. Also, this is the period at which changes are taking place in the relative positions of Schlemm's canal, the angle and the ciliary body. It seems possible, therefore, that the disturbance at this time may have been the ætiological factor in the occurrence of buphthalmos.

Summary.

1. A case of bilateral buphthalmos in which the tension was reduced to normal by goniotomy is described.
2. The possible relationship between the occurrence of buphthalmos and operation for "fibroid" at the fifth month of pregnancy is noted.

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CONGENITAL STENOSIS OF THE PULMONARY VEINS IN THEIR EXTRAPULMONARY COURSE.

By R. D. K. REYE, M.D. (Sydney).
From the Department of Pathology, Royal Alexandra Hospital for Children, Sydney.

DEVELOPMENTAL ABNORMALITIES of the pulmonary veins, in their extrapulmonary course, have been recorded on a number of occasions. Such records deal with anomalous pulmonary veins which enter the heart at some point other than in the left auricle, or which make connexion with the heart only by an indirect route. The literature concerning this type of maldevelopment is summarized, up to 1944, by Compere and Forsyth (1944), and these authors include in their paper a discussion of the embryological development of these veins. A search of the English and American literature has failed to reveal any case similar to the one to be described, which would seem to be of considerable rarity.

Clinical Record.

The patient, a girl of eight years, was known to have some form of congenital defect of the heart, but little is known of her medical history before her admission to hospital, except that she was prone to develop periods of stupor from which she could not be roused and that her pulse rate was continuously elevated. At the time of her admission to hospital evidence of congestive cardiac failure was already apparent. There was œdema of the legs and sacrum and the liver was enlarged. During her six weeks' stay in hospital, up to the time of her death, her heart rate remained persistently elevated and in the vicinity of 140 beats per minute. The blood pressure, estimated on one occasion only, was recorded as 70 millimetres of mercury, systolic, and 50 millimetres, diastolic. A skiagram of the thorax showed gross cardiac enlargement, principally of the right ventricle.

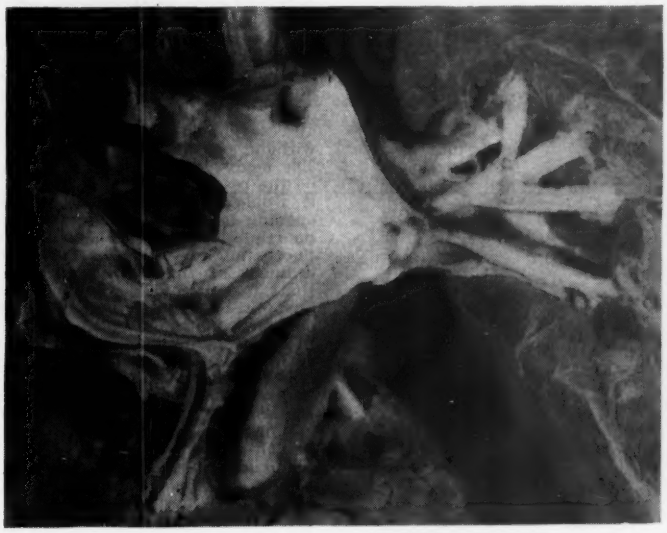

FIGURE I.

The left auricle has been opened. Just off centre and to the right are the openings of the two pulmonary veins from the left lung; the lower vein has been opened throughout its length. The veins from the right lung are situated below and to the left of centre. Natural size.

Autopsy Findings.

The significant autopsy findings were restricted to alterations in the heart and lungs.

The heart was greatly enlarged owing to right ventricular hypertrophy and dilatation. The right auricle, too, was much enlarged, while the left auricle and left ventricle were relatively small and absolutely smaller than is normal. The endocardium of the right auricle and ventricle was slightly thickened, white and opaque, and the tricuspid and pulmonary valves were thick and fleshy. An enlargement, comparable to the increased size of the right ventricle, was noticeable in the pulmonary artery. The main stem of this vessel had an outside diameter of 1·6 centimetres, compared with an outside diameter of 1·0 centimetre for the aorta at the same level. The wall of this enlarged pulmonary artery was thick and firm, and there was evidence of hypertrophy of all the branches of this vessel within the lungs. These arteries stood out prominently on the cut surfaces of the lungs, and though no atheroma was visible in the main stem of the vessel, yellowish plaques were visible in the larger pulmonary arteries within the lungs. The lungs were fully expanded, heavy, firm and subcrepitant. The lower lobes were dark red, but the middle and upper lobes on the right side and the upper portion of the upper lobe on the left side were creamy white, with a mesh of fine, tortuous vessels visible beneath the visceral pleura.

The Left Auricle and Stenosed Pulmonary Veins.—When viewed from the inner aspect there could be seen, in the wall of the left auricle, three minute orifices in situations corresponding to those normally occupied by the mouths of pulmonary veins. The higher of the two orifices on the left side, shown on the right side of Figure I, would just admit a coarse bristle, and this could be passed into the vein for a distance of 0·5 centimetre. Beyond this, to a point just proximal to the junction of the three tributary veins, the lumen of the vessel was too narrow to admit even a fine hair; Figure II, a cross-section of the vessel at this level, shows the minute lumen which was present. Distal to this narrowed part, that is toward the hilum of the lung, the lumen of the main vein and of the three tributaries was of normal calibre. It is possible to distinguish between the stenosed and normal portions of this vessel by reference to Figure I, since the walls of the veins have collapsed in those parts in which the lumen is fully developed. The vein draining the lower lobe on the left side, shown below and to the right in Figure I, was opened throughout its length. This vein had a wide lumen, but entered the auricle by a constricted orifice, and the ridge of tissue which encircled the mouth of this vein to produce stenosis of it is still apparent in the figure. The veins draining the right lung, shown to the left and below in Figure I, were affected in a manner similar to those on the left side. There was one exception, however, in that the vein draining the middle and upper lobes did not reach to the auricular wall. To outward inspection this vein seemed to empty into the vein coming from the lower lobe, but when a probe was passed into the lumen it could be shown that no such communication existed between these two veins and that, in fact, the vein from the upper and middle lobes ended blindly.

Discussion.

It is assumed that the stenosis of the mouths of three pulmonary veins and the atresia of the orifice of one pulmonary vein are of congenital origin. This assumption does not seem ill-founded and is compatible with the little that is known of the patient's history. There is no evidence to suggest a post-natal inflammatory origin for the stenosis, nor does thrombosis seem to have played any part in

instituting or propagating these lesions. In the cross-section of the vein which was narrowed for a distance beyond its orifice (Figure II), the histological pattern does not suggest that the narrowing is due to organized thrombus, for the tissue which encircles the lumen consists principally of widely separated bundles of smooth muscle.

A congenital defect of the type depicted here would throw no additional burden on the heart during fœtal life. It did produce alterations in the circulation after birth of the kind which would be expected from it. The atheromatous changes in the pulmonary arteries, too, are not without interest, since this case supplies a clear-cut example of atheroma developing in vessels subject to increased stress and occurring in a young child in whom no infectious disease or known metabolic disorder would seem to have complicated the illness.

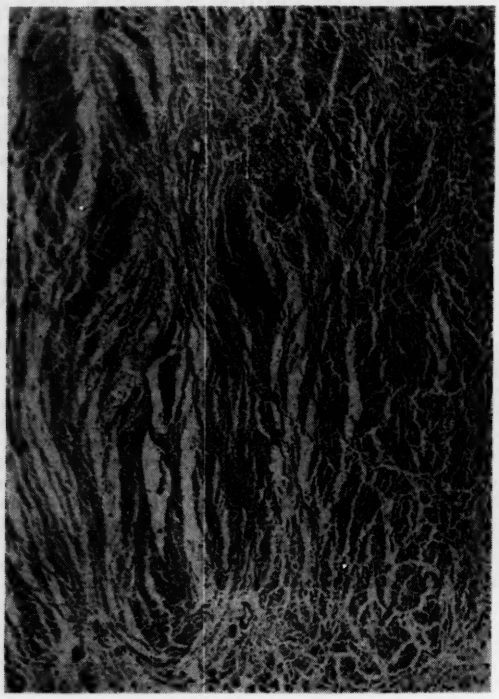

FIGURE II.

Transverse section of vein draining upper left lobe. Section made 0·3 centimetre distant from auricular orifice. A small, eccentrically placed and divided lumen can be recognized. Hæmatoxylin and eosin stain × 100.

Summary.

A case is described in which congenital stenosis of the orifices of the pulmonary veins resulted in right ventricular hypertrophy and ultimately in congestive cardiac failure. Atheroma was well advanced in the pulmonary arteries within the lungs, but was absent from the arteries in the systemic circuit.

Acknowledgement.

The patient was under the care of Dr. R. Taylor, to whom I am indebted for the clinical history.

Reference.

Compere, D. E., and Forsyth, H. F. (1944), "Anomalous Pulmonary Veins", *The Journal of Thoracic Surgery*, Volume XIII, page 63.

Reviews.

PROCTOLOGY IN GENERAL PRACTICE.

"PROCTOLOGY IN GENERAL PRACTICE" by Nesselrod will be a useful book for the general practitioner.[1] The subject is well covered, the book is clearly set out, and the illustrations, especially those in colour of proctological and sigmoidoscopic findings, are excellent.

In keeping with present North American teaching, stress is laid on the place of infection of the anal ducts and glands in the ætiology of most ano-rectal conditions; and there are several other points, as is to be expected, which differ from the teaching and practice in Australia. Little use is found for the injection treatment of hæmorrhoids, and in those cases in which it is used each injection is preceded by one or two small enemata, the injection is given into the centre of the group of varices, and quinine and urea are used as the sclerosing agent. The Buie position is advised for anal operations, and it is recommended that these operations be followed by para-anal injections of oil-soluble anæsthetic agents despite the acknowledgement that abscesses and sloughing are likely to occur.

The anatomical studies of the anal musculature of Peter Thompson at the beginning of this century and then later by Milligan *et alii* have received little recognition. The muscle labelled "Internal Sphincter" in Figure 63 is undoubtedly the subcutaneous part of the external sphincter.

The advice is given that "the incision into an ischiorectal abscess should be as near as possible to the anal margin without sacrifice of observance of the 'point of fluctuation'. The nearer the opening to the anal margin the shorter will be the resultant fistulous tract." This is no doubt true, but it would be better to recommend including the internal opening into the bowel in the incision so that there will be no resultant fistulous tract. Surely one does not wait for fluctuation to open an ischio-rectal abscess! In regard to drainage of an ischio-rectal abscess the statement is made that "the surgeon is careful, of course, to avoid sectioning any fibres of sphincteric musculature when cutting towards the anal margin". That part of the sphincter superficial to the tract of an anal fistula must be divided to cure the fistula, and this is mentioned further on. Other points with which one might differ are that preparation for sigmoidoscopy with repeated enemata is advisable as a routine measure, that bleeding is the most important early symptom of carcinoma of the rectum (rather than an alteration in bowel habit), and that there is much the modern radiologist can do to aid in the management of malignant disease of the rectum. It is also felt that complications other than stricture and polypus formation should have been mentioned in the discussion on chronic ulcerative colitis.

However, apart from these minor criticisms it must be repeated that this book will be a very useful guide for the general practitioner and others who do not already possess a recent book on proctology.

"JOHN HUNTER, THE SURGEON-NATURALIST."

ONE essential preliminary to a study of the main factors which started modern surgery upon its unerring path of progress in the eighteenth century would need to be a careful investigation of the life and work of John Hunter. In a short biographical sketch,[2] Dr. S. Roodhouse Gloyne, consulting pathologist to the London Chest Hospital, has given an excellent account of the paths taken by this remarkable scientist in all matters pertaining to the study of medicine and natural history. In the telling of his story Dr. Roodhouse Gloyne has used a scholarly method of presentation, a fluent style and a wide knowledge of the period in which the various scenes are set.

It would seem that the career of John Hunter was unorthodox even for those times, when medical education was a thing of shreds and patches and public hospitals

[1] "Proctology in General Practice", by J. Peerman Nesselrod, B.S., M.S., M.Sc. (Med.), M.D., F.A.C.S., F.A.P.S.; 1950. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9¼" × 6", pp. 300, with many illustrations. Price: 57s.

[2] "John Hunter", by S. Roodhouse Gloyne, M.D. (Leeds); 1950. Edinburgh: E. and S. Livingstone, Limited. 8¾" × 6¼", pp. 144, with some illustrations. Price: 15s.

were becoming fastidious about the qualifications of medical or surgical specialists seeking appointments on the staff. So far as can be ascertained, the young Scotsman never in his life sat for an examination to qualify in any branch of medicine. He was twenty years of age before circumstances compelled him to join his brother, William, in London, where he learned to dissect parts for demonstration in the private school of anatomy, without entering into any formal contract of apprenticeship in the prescribed manner of the day. And, strange as it may seem, he had lectured with Percival Pott as Master in Anatomy at Surgeons' Hall, had obtained the appointment as an honorary surgeon on the staff of Saint George's Hospital, and had been elected a Fellow of the Royal Society, all before he received the diploma as a member of the Corporation of Surgeons in London.

There can be no doubt, after reading this book, that the influential backing of his brother and a few other friends had enabled John Hunter to reach eminence in his profession by such a devious and unfrequented route. Even so, the main factors concerned in his progressive march to fame were his penetrating studies of human anatomy and the tireless energy and thoroughness with which he pursued the investigation of structure and function in any living creature, always hoping to find some application of his researches to the human body in health or disease. The ultimate course of his career makes it appear that in his case the regular routine of medical education and training was altogether unnecessary; without it he was able to advance the science and art of surgery and to point the way for future medical research.

The names of William and John Hunter are writ large in the annals of medical history, but few modern surgeons are really conversant with the actual achievements and methods of research which gave these names to posterity. This small volume gives a clear picture of the younger brother; it is well illustrated and the general format is a credit to the publishers.

ADVANCES IN GYNÆCOLOGY.

"PROGRESS IN GYNÆCOLOGY", Volume II, follows the general plan of Volume I with 78 contributors.[1] Many of the chapters are merely revised by the original authors, while other subjects are dealt with by new contributors, not only from America but also from England and Europe.

Cancer of the cervix is dealt with in great detail and an endeavour is made to assess the various improved techniques, both radio-therapeutic and surgical. Brunschwig and Pierce report on the work in progress of partial and complete pelvic exenteration in advanced pelvic cancer.

A new author, Charles Read, reviews adequately the varied surgical techniques used in the cure of stress incontinence. A useful chapter on blood control in gynæcological conditions is included as well as Kegel's work on active exercise of the pubo-coccygeal muscle showing the importance of the syndrome of "lack of awareness of function and coordination of the pelvic muscles".

The inclusion of larger bibliographies is an advantage in many chapters.

THE RADIUM TREATMENT OF MALIGNANT DISEASE.

THE third volume of Stanford Cade's "Malignant Disease and its Treatment by Radium" follows the pattern of the preceding volumes.[2] A lucid account of the pathology, predisposing factors, and theories of causation of carcinoma in the various sites is of special value to those interested in the problem of malignant disease.

This volume is concerned mainly with carcinoma of the breast and genital tract, but includes also discussions on malignant disease of œsophagus and stomach, rectum and anus and intrathoracic tumours which have been contributed by various authors.

Carcinoma of the cervix has been dealt with in an admirable manner. Both the Paris and Stockholm techniques and their various modifications have been described. An important section gives the contraindications to radium treatment and the various complications that may arise, with methods of prevention and treatment. Rectal reactions are not uncommon, but could be avoided by scrupulous attention to details of technique. A comparison of results of radiotherapy in carcinoma of the cervix since 1936 shows that there has been a steady improvement in results, but that it is not yet possible to correlate this improvement with the various techniques employed.

Although treatment by radium has been the chief method described throughout the volume, X-ray therapy has not been neglected and mention is also made of supplementary therapeutic methods which may prove of value. Among these are the use of œstrogen and the androgens in carcinoma of the breast and of radioactive sodium in the treatment of carcinoma of the bladder.

RECENT PROGRESS IN PSYCHIATRY.

PUBLISHED by authority of the Royal Medico-Psychological Association, "Recent Progress in Psychiatry" contains a great deal of well-documented and critically handled material from current psychiatric and neurological literature.[1] This is the second edition of the work and is apparently a special issue of *The Journal of Mental Science*; it covers the immediate post-war period. The editor, G. W. T. H. Fleming, states in his introduction that a third edition, due in 1955, will include chapters on child psychiatry, psychopathic personality, manic-depressive insanity, convulsion therapy, and anatomy. These subjects are not specially dealt with in the present volume, which contains articles, each by a British author of standing, on psychiatric genetics, biochemistry of the nervous system, electroencephalography, cybernetics, vitamin deficiency in nervous and mental disorder, physiological psychology, neuro-endocrine relationship and endocrinology in clinical psychiatry, intelligence testing, personality tests, psychopathology, neuropathology in relation to mental disease, the neuropathology of oligophrenia, schizophrenia, problems of old age and the senile and arteriosclerotic psychoses, neurological psychiatry, neurosyphilis and its treatment, epilepsy, mental deficiency, delinquency and crime, sleep and its disturbances, psychotherapy, insulin therapy, the neurosurgical treatment of mental illness, and suicide. Extensive bibliographies and a general index add to the reference value of the book, which will be of use to psychiatrists, neurologists, neurosurgeons and many others with an interest in these subjects.

GENERAL PSYCHOPATHOLOGY.

THE first half of the book, "Principles of General Psychopathology", by Siegfried Fischer, is devoted to a discussion of the terms used in general psychology.[2] This account includes a definition of the terms, their mechanism of production and the disorders in which they most frequently occur. Here are considered perception, delusions, disorders in memory and thought processes, attention, orientation, emotion and the drive of the individual. Then follow a discussion and interpretation of these processes in terms of dynamic psychology. The final chapters give a very brief review of personality structure and its deviation from normal. The description of the different terms used is clear, but the explanation of their mechanism is not very satisfactory. Words and phrases are used which are at times confusing

[1] "Progress in Gynecology", edited by Joe V. Meigs, M.D., and Somers H. Sturgis, M.D.; Volume II; 1950. New York: Grune and Stratton, Incorporated. 9" × 6", pp. 842, with many illustrations. Price: $9.50.

[2] "Malignant Disease and its Treatment by Radium", by Sir Stanford Cade, K.B.E., C.B., F.R.C.S., M.R.C.P., with a foreword by Sir Ernest Rock Carling, F.R.C.P., F.R.C.S., F.F.R.; Volume III; Second Edition; 1950. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall, Limited. 9" × 6", pp. 458, with 182 illustrations, some of them coloured. Price: 52s. 6d.

[1] "The Journal of Mental Science (The British Journal of Psychiatry): Recent Progress in Psychiatry", by authority of the Royal Medico-Psychological Association, edited by G. W. T. H. Fleming in collaboration with Alexander Walk and P. K. McCowan; Second Edition. London: J. and A. Churchill, Limited. 9" × 6", pp. 717. Price: 50s.

[2] "Principles of General Psychopathology: An Interpretation of the Theoretical Foundations of Psychopathological Concepts", by Siegfried Fischer, M.D.; 1950. New York: Philosophical Library, Incorporated. 8½" × 5½", pp. 356. Price: $4.75.

and difficult to understand. Also, the author's "dynamic interpretation" is not very clear. Generally the book provides a satisfactory description of the terms used in psychopathology, but it does not give a clear account of the principles of general psychopathology.

HAY FEVER.

JOHN FREEMAN's "Hay Fever" is a most unusual text-book[1] and although it will be read with delight by many of those especially interested in the so-called "allergic diseases", it is likely to exasperate the busy general practitioner who is looking for a comprehensive and compact book on the investigation and treatment of hay fever.

With Leonard Noon, Dr. Freeman in 1911 originated the methods of treating hay fever by injection of extracts of allergens and every page of this book reflects his originality and vast experience. Like Sir Almroth Wright, in whose laboratory he worked, he has a "well developed taste for scientific neologisms", but many of his terms (toxic idiopathies, idiotoxin, idioceptor, para-hay fever, pathophane, *et cetera*) have not found their way into a majority of text-books. He is justifiably concerned at the misuse of technical terms and particularly distrusts the modern usage of the term "allergy". However, few will agree that one individual can resolve the confusion by coining still more terms. In discussing causal mechanisms, he rightly points out that it is a common fallacy to assume only one cause for a disorder; more commonly at least two factors combine to cause the illness.

One of the greatest disadvantages of treatment of allergic conditions by "desensitization" is the tedious series of injections required, and Freeman and his team have overcome this difficulty to some extent by the somewhat unorthodox device of teaching patients to give their own injections.

Dr. Freeman is keenly aware of the importance of studying the psychology and emotional condition of his patients and has some especially shrewd digs at possessive parents who will not allow their children to grow up, and at those extremist psychiatrists who are obsessed by certain limited aspects of psychology and who sometimes do more harm than good.

In addition to the Table of Contents, he has a list of "Case Histories and Anecdotes" and it is these which will please those with a sense of fun, adequate leisure and not too keen a hunger for concentrated scientific disquisition. Such items as "The Boxing Cadet", "The Wayward Cat", "The Marmite Lady", "Flat Eggs", "Dog-dust Girl", and "Rash Oxford Scientist" whet the appetite. Dr. Freeman has evidently enjoyed his forty years of research and practice and writes with zest and a lack of inhibitions which is both unusual and pleasing. He admits that the book took many years to write and devastated so many holidays for his wife, friends, children and (ultimately) grandchildren, that it became known as "The B.B."—"That Bloody Book".

Asthma, dermatitis and urticaria, although mentioned incidentally, are not discussed in detail nor is there any comprehensive section on the immunology of allergic diseases. The book is well printed and contains several interesting illustrations, including a portrait of Leonard Noon who died, aged thirty-five years, shortly after his poineer work was published.

Notes on Books, Current Journals and New Appliances.

"VACUUM."

EVERY advance in the technique for the production of a high vacuum is followed before long in almost every field of industry and science by important developments yielding new methods, materials and discoveries. In order that these advances may be brought to the notice of scientists in industry a new journal, *Vacuum*, has been established. The first issue bears the date January, 1951, and it will appear once a quarter. The journal is described as "a review of developments in vacuum research and engineering". The first number consists of a contributory section of articles from international specialists and a section devoted to abstracts. Other series will be added when the need for them becomes apparent. The original articles in this number comprise one on the services of vacuum, a second which is a review of a laboratory freeze drying with particular reference to viruses, and a third deals with the production, properties and uses of thin films condensed *in vacuo*. The journal is published by W. Edwards and Company (London), Limited, Worthley, Bridge Road, Lower Sydenham, London, S.E.26. The subscription is £1 5s. *per annum* in England and £1 10s. abroad. This journal may find a sphere of usefulness in certain medical laboratories and institutes of research.

[1] "Hay-Fever: A Key to the Allergic Disorders", by J. Freeman, D.M. (Oxon.); 1950. London: William Heinemann (Medical Books), Limited. 9¼" × 7¼", pp. 348, with illustrations. Price: 42s.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Nasal Sinuses: An Anatomic and Clinical Consideration", by O. E. Van Alyea, M.D.; Second Edition; 1951. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" × 6", pp. 342, with 143 illustrations, some in colour. Price: £4 16s. 9d.

The book is devoted to subjects likely to interest rhinologists as a whole and is based on the author's anatomical studies.

"Antenatal and Postnatal Care", by Francis J. Browne, M.D. (Aberdeen), D.Sc., F.R.C.S. (Edinburgh), F.R.C.O.G.; Seventh Edition; 1951. London: J. and A. Churchill, Limited. 8½" × 5½", pp. 712, with 94 illustrations. Price: 30s.

An extensive revision of the edition published in 1946.

"A Handbook of Ophthalmology", by Humphrey Neame, F.R.C.S., and F. A. Williamson-Noble, F.R.C.S.; Seventh Edition; 1951. London: J. and A. Churchill, Limited. 9½" × 6¼", pp. 350, with 13 plates, containing 46 coloured illustrations and 155 text figures. Price: 22s. 6d.

Intended as an "elementary" text-book—reference to rarer developments in ophthalmology have been omitted.

"Infant Feeding and Feeding Difficulties", by Philip Rainsford Evans, M.D., M.Sc., F.R.C.P., and Ronald MacKeith, M.A., D.M., M.R.C.P., D.C.H.; 1951. London: J. and A. Churchill, Limited. 8" × 5¼", pp. 264, with 64 illustrations, including two coloured plates. Price: 12s. 6d.

Intended for students and practitioners and also for nurses, health visitors and others.

"Contraceptive Technique: A Handbook for Medical Practitioners and Senior Students", by Helena Wright, M.B., B.S. (London), and H. Beric Wright, M.B., B.S. (London); 1951. London: J. and A. Churchill, Limited. 7½" × 5", pp. 78, with 16 illustrations. Price: 6s.

Intended as a guide to practitioners in the treatment of their patients.

"Serum Sickness", by C. Frh. von Pirquet, M.D., and Bela Schick, M.D., translated by Bela Schick, M.D.; 1951. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" × 6", pp. 142, with 33 charts. Price: 38s. 3d.

A translation of the book first published forty-five years ago.

"Incontinence in Old People", by John C. Brocklehurst, M.D., with a foreword by Stanley Alstead, M.D., F.R.C.P.; 1951. Edinburgh: E. and S. Livingstone, Limited. 10" × 7", pp. 204, with 62 figures. Price: 30s.

The incontinence dealt with is incontinence of urine and fæces. The author deals with causation and treatment.

"The 1950 Year Book of Orthopedics and Traumatic Surgery (November, 1949-November, 1950)", edited by Edward L. Compere, M.D., F.A.C.S.; 1951. Chicago: The Year Book Publishers, Incorporated. 7¾" × 5¼", pp. 388, with 264 figures. Price: $5.

One of the "Practical Medicine Series" of year books.

The Medical Journal of Australia

SATURDAY, JUNE 2, 1951.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

SCIENCE IN BONDAGE.

In Berlin on June 27, 1950, Dr. H. J. Muller, of the Department of Zoology, Indiana University, a well-known authority on genetics, delivered a very outspoken address entitled "Science and Totalitarianism", in which he attacked with considerable vehemence the treatment of his particular branch of biological science in Russia. This address formed the basis of an article by the same author entitled "Science in Bondage", published in the American journal *Science* of January 12, 1951. Dr. Muller makes statements concerning the necessity for freedom in scientific inquiry with which all thinking men in democratic countries will agree. Science must be detached from the despotism of imposed ideas and, most important of all, there should be "a spirit of inquiry and objectivity, a wide tolerance for objectively reached but conflicting conclusions of others, a custom of candid criticisms, a distrust of all argument by authority and of all wishful thinking". A terrible picture is given of the persecution of certain Russian researchers in genetics, for apparently their conclusions were not acceptable to the Soviet authorities. These geneticists were "subjected to a continuous sniping process and to two more staged tournaments, one in 1939 and the last in August, 1948. By the latter date all the noted names of Russian genetics had disappeared; the great Vavilov had perished in a labour camp in Siberia and many others whose memory I hold dear had lost their lives in unexplained ways. Thus only a feeble remnant of comparative weaklings in the science was left to defend or compromise it. . . . Beginning in 1936 a series of attacks upon genetics was instituted. These ranged from deliberate misrepresentations and vilifications in the Press to forced confessions of error and guilt from some of the leading geneticists, followed by their disappearance and the closing of their laboratories. . . . About the same time, because no real scientist could be found to attack genetics, this assignment was delegated to a half-educated and paranoic young demagogue named Lysenko, who had done some work in raising plants, but who was in fact ignorant of scientific principles and incapable of understanding them. Lysenko's reputation was systematically inflated before the public eye and he was provided with a sophisticated interpreter of dialectical materialism, a cynical weaver of words named Present, so that Lysenko's crudities might be disguised and served up to the public as profundities. . . . At the same time the laboratories of genetics were closed, their remaining workers were somehow disposed of, courses on genetics were abolished and all books on the subject were banned."

The trouble is that the science of genetics has developed a formidable terminology which can be understood only by experts in this field, and many of the conclusions are presented in a manner not comprehensible to the ordinary intelligent reader even when possessing some biological knowledge. A more favourable estimate of Lysenko appears in a book, "The Science of Heredity", which has just reached Australia.[1] Here the author, J. S. D. Bacon, M.A., Ph.D., a lecturer on biochemistry in the University of Sheffield, writes as follows: "There is no doubt that Lysenko's work and the theories which he bases on it have been ignored unjustifiably by most geneticists, both in his own country and abroad. It would seem to the author that there can be no satisfactory development of the science beyond its present stage until his ideas have been considered seriously, particularly from the experimental point of view, and some serious answer made to his criticisms of modern genetics." Possibly Dr. Muller would accuse Dr. Bacon of "red" sympathies and might also find dialectic satisfaction in the fact that Dr. Bacon is a biochemist who has never carried out any research in genetics. It is possible to avoid the heat of controversy and vituperation and to make some sort of a calm review of the position. Apparently Lysenko, supported by his school, has had some undoubted and even striking successes in practical plant breeding, but he is not well versed in general theory and has gone too far in attacking what he has not properly understood. But whether Lysenko is right or wrong there can be no doubt that strong political pressure, backed by police action, has been brought to bear on men of science in Russia, in countries of its satellites and in Germany east of the "Iron Curtain". Against this curtailment of scientific freedom we will all protest with vigour.

It might be considered that modern medicine remains singularly exempt from political or ecclesiastical restraint. Yet if Dr. Muller is correct, Soviet totalitarianism has entered the field of medicine. "The germ theory of disease and the work of Koch have been derided by the party-sponsored theory of disease of Speransky, which attributes most ailments to malnutrition of the nervous system." It will not do the germ theory any harm to be attacked so long as the attack is conducted along scientific lines and is free from political or social pressure. Universities and technical schools receive money from governments, corporations and private companies and individuals, but if such gifts are coupled with the condition that the conclusions announced must conform with certain political, economic or religious doctrines, then the assistance should be emphatically refused. Science, including medical science, has of course suffered from the self-imposed authoritarianism which too often arises from reverence of the

[1] "The Science of Heredity", by J. S. D. Bacon, M.A., Ph.D.; 1951. London: Watts and Company. 6¼" × 4¼", pp. 200, with many illustrations. Price: 3s. 6d.

greatness of one single man. It is admitted that Newton's supremacy in mathematics hindered the expansion of this science in Britain during the latter part of the eighteenth century, and had Clerk Maxwell been a smaller man he might have hesitated to go counter to the mechanical physics of Kelvin. Even Lister's advocacy of the spray required some courage to oppose. But such conservatism is of short duration and is happily rare. There is, however, one great question which is agitating thinking men, in the English-speaking world particularly. In the words of Professor Chauncey Leake, of the University of Texas: "How can we obtain the advantages of social unity whilst at the same time preserving individual freedom . . . . We must go on and on all the time in guiding, training and leading our youngsters to understand the democratic principle." At present the danger to medicine is slight, but that should not blind us to the possibility of a sudden emergence of politically or socially or religiously directed indoctrination which would assuredly lead to disaster. If medical science does not go forward it must go backwards, and freedom is the very life blood of its progress.

Current Comment.

PSYCHOSOMATIC NON-ARTICULAR RHEUMATISM.

THE symposium has long been a favourite mould from which may be cast an image of a scientific subject, so that it may with profit be viewed from all angles. It must, of course, be admitted that only partial views may yet be obtained of many subjects in clinical medicine; of these subjects the vague term "chronic rheumatism" is a good example. If we except from this class of malady the articular rheumatic affections there remain still many disorders, which comprise, so it is said, some 75% of all varieties of chronic rheumatic disorders. This estimate is given by Phillip Ellman and David Shaw in an article on the psychosomatic aspects of non-articular chronic rheumatism.[1] It is well known that "backs, bellies and heads" formed a good proportion of the ailments bringing servicemen to the sick parade, and in the civil community the same occurs. Many writers have reported on investigations into the emotional factors concerned in perpetuating, if not producing, pain and stiffness which may annoy, depress or even cripple men and women in reasonable health. Ellman and Shaw quote the American finding that 15% to 20% of servicemen investigated in rheumatism centres suffered from a psychoneurosis, "a musculo-skeletal expression of functional disorders". In their own investigation they studied 109 patients, 78 women and 31 men, over a period of four years. They were drawn chiefly from artisans, and their average age was forty-four years. They all had attended a rheumatism clinic for at least six months. A diagnosis of non-articular chronic rheumatism was made by exclusion, after full clinical, pathological and radiological examination. Similar investigations were made of 34 women and 24 men of comparable age and social class who were used as controls. All the patients in the series complained of pain and stiffness, chiefly localized: in one-third of them the location was the back. Right-sided pain was commoner than left-sided, but not to a significant extent. Associated symptoms were present in nearly half the patients, such as loss of sleep, depression and headache. In all there was a striking disparity between the troublesome nature of the symptoms and the paucity of the physical findings. Every patient was examined psychiatrically, and evidence sought of neurotic features, such as a history of instability in the family or during childhood, or, in later years, emotional conflict, or personality aberrations. Such a history was obtained in 49% of cases among these chronic rheumatics, but only in 14% of the controls. Early breakdowns were found in 48%, but only in 21% of controls. Emotional stress of a type and severity considered significant as a precipitating factor was found in 27%, but in only 11% of the control series. Nearly 80% of the patients showed evidence of a significant personality disturbance, or even frank neurosis. Analysis showed that the majority of these patients fell into three personality groups, the over-anxious, the inhibited and the obsessional, and the familiar tension of the anxiety state was in evidence in nearly half of them. As might be expected, the localizing influence of previous injury or disease, both in the patient himself and in members of his family, was found to be of some importance.

The authors point out the important implications of these findings on diagnosis and treatment. It is interesting that they found that a number of patients had failed to gain relief from physiotherapy, but many were suitable for psychotherapy as out-patients. Ellman and Shaw rightly stress the danger of "fixing" the symptoms; it is highly probable that in many people with psychosomatic disease fixation has already occurred before a complete review of their state can be given. Perhaps one of the most useful purposes served by such contributions to literature is that of minimizing the real dangers of fixation, though how this is to be done in an increasingly mechanized world is becoming one of the major problems of medicine today.

[1] *Annals of the Rheumatic Diseases*, December, 1950.

AUREOMYCIN.

AUREOMYCIN has become established as one of the most useful of antibiotics, and detailed studies of its use, such as that recently presented by C. M. Whitlock, A. D. Hunt and Sylvia G. Tashman[1] on its administration to children, will be generally welcomed. From Whitlock, Hunt and Tashman's study it appears that aureomycin in doses of approximately 11 milligrammes per kilogram of body weight given orally at four-hourly intervals is well tolerated by the great majority of infants and children. Although highly variable, the serum levels resulting from such a dosage schedule are generally at or above the effective in-vitro inhibitory concentration for most sensitive organisms. In addition, patients suffering from most of the bacterial, viral, rickettsial, spirochætal and protozoan infections reported as being treated successfully with aureomycin have been treated with oral dosage schedules roughly comparable with the one mentioned here with or without small intramuscular supplementary doses. Single doses larger than 11 milligrammes per kilogram of body weight do not appear to produce significantly higher serum levels. For this reason a large initial "booster" dose has not been used. Smaller individual doses or more infrequent doses may prove satisfactory in many cases. The same total daily dose (60 milligrammes per kilogram of body weight) divided into individual doses given at a lesser frequency than every four hours may or may not prove equally effective and well tolerated; this point cannot be determined from the data in the present study. For patients unable to take aureomycin by mouth, and with infections requiring intensive treatment and high serum levels, the intravenous route seems to be the most desirable method for parenteral administration. The tentative dosage schedule of 6·6 milligrammes per kilogram of body weight given intravenously every twelve hours seems reasonable. A single intravenous dose of aureomycin of 6·6 milligrammes per kilogram of body weight, followed thereafter by oral administration of aureomycin, may be desirable at times. The occurrence of frequent febrile reactions, local pain and inflammation, as well as poor serum levels, has dissuaded Whitlock, Hunt and Tashman from using the intramuscular route; and so far as can be judged from the limited data, rectal administration seems too unreliable for routine use, whether or not water is added to enhance the absorption. The presence of aureomycin in the spinal fluid of children with non-inflamed

[1] *Pediatrics*, December, 1950.

meninges receiving aureomycin by the oral route suggests that intrathecal administration of aureomycin should be unnecessary in the treatment of meningitis, but this is not the sort of point that can be determined certainly without considerable clinical and/or experimental trial. The organisms highly sensitive, moderately sensitive and relatively resistant to aureomycin are listed in the paper, which should be consulted by those interested in this aspect. On the subject of alimentary absorption, it is pointed out that after a single oral dose the serum level reaches a low peak in one to four hours, and this level is maintained for six to eight hours after ingestion of the drug. After intravenous injection a prompt peak level is followed by a rapid fall. It seems, therefore, that alimentary absorption proceeds regularly and slowly for several hours. Milk does not interfere with this absorption, and it decreases the tendency to nausea, vomiting, abdominal pain and diarrhœa. The relatively low peak values for aureomycin after intravenous injection, as compared with streptomycin and penicillin, suggest that aureomycin, unlike these other drugs, is distributed fairly uniformly throughout the body, rather than confined mainly to the extracellular fluid. Rapid destruction, rapid excretion and serum-protein binding seem to be ruled out as possible causes of this low peak in serum values. The precise mode of renal excretion is not known. However, the slow rate of disappearance of aureomycin from the serum, *plus* the fact that carinamide in doses known to block the tubular excretion of penicillin does not affect the slopes of the aureomycin serum level curves, suggests that tubular excretion plays a negligible part and that renal excretion is glomerular alone.

This paper commends itself in at least two ways. Firstly, it offers practical data to guide the clinician in his use of a valuable therapeutic agent. Secondly, it contributes to and so helps to stimulate the study of dosage in pædiatric practice. In the last two volumes (1949 and 1950) of "The Year Book of Pediatrics", the editor, H. G. Poncher, has pointed out the inadequacy of older methods of determining dosage for children and the need for studies of dosage of individual drugs that get away from the false ideas that the child is in this respect a miniature adult and that generalizations can be made from the effectiveness of one drug to that of drugs of similar action. Whitlock, Hunt and Tashman's study contributes towards this need.

EXHAUSTION IN THE YOUNG BUSINESS EXECUTIVE.

IT seems to be generally assumed that with present-day hours and conditions of work and remuneration the "white collar" worker does quite well. Men or women at the executive level are rarely thought, either by their employers or by themselves, to be subject to anything in the nature of an industrial hazard. That this is a rose-coloured view will be supported by many general practitioners, physicians and psychiatrists who have had people of this group under their care, and more precise information on the matter has been assembled by S. A. Portis, I. H. Zitman and C. H. Lawrence[1] from their own and other investigations. Particular emphasis is laid on exhaustion states developing in young business executives, these being typically young men of ability and education who "started out in their jobs with all the zest and enthusiasm and ambition to reach a goal which would give them prestige, affluence and security" and then in their early forties or fifties became utterly exhausted, with loss of enthusiasm and even antipathy to their work, business superiors and associates. Portis, Zitman and Lawrence found that of an unselected consecutive group of 50 business executives under the age of fifty years who consulted them as patients, two-thirds had fatigue as an outstanding complaint. This complaint, they agree, is difficult to evaluate, but they found that more than two-thirds of the fatigued group had relative hypoglycæmia, and this they regard as clinically significant. They offer evidence to suggest that the origin of the disturbance causing hypoglycæmia is in the emotional centres of the central nervous system and that an inadequate blood sugar level contributes to faulty brain function, fatigue and general inefficiency. Psychological studies, it is stated, show that executives with somatic symptoms are usually dependent men with a strong sense of inadequacy and inferiority; to this they react with their drives to succeed. They tend to develop somatic symptoms, and though their business interpersonal relations appear adequate on the surface, their families suffer. Their capacity for getting pleasure out of life is limited. A significant point is their fear of failure, this because of loss of pride more than loss of material things.

For comparison purposes Portis, Zitman and Lawrence studied 55 executives under the age of fifty years who had been referred to them by the executives' employers for prophylactic examination. In this group only six of the 55 appeared to be suffering from fatigue, but the majority had significant though asymptomatic physical defects. Many of these would no doubt have sought medical advice sooner or later, and probably by then a higher proportion of fatigue would have been evident, so that the low figure in this group does not warrant underestimating the problem's importance. It is pointed out that the stress and strain of superimposed emotional factors on well-balanced organic defects give rise to symptoms which cause the patient to seek medical care. Early detection and correction of organic defects should then aid in preventing development of exhaustion states, apart from the ultimate general benefit to the patient. The management of emotional problems will perhaps require psychiatric aid in some cases. Portis, Zitman and Lawrence seem undecided whether the matter is one for the psychiatrist or the personal physician. In this country the weight of opinion would almost certainly favour leaving the matter in the hands of the personal physician unless he desires specialist help—provided always, of course, that the physician is of the wise type that appreciates the psychological factors in his general assessment of the patient. Apart, however, from organic defects and emotional problems, these investigators put forward certain other factors that they regard as particularly relevant. The first is that of unsatisfactory eating habits, especially inadequate and hurried breakfast and luncheon with consequent development of hypoglycæmia as the morning or afternoon progresses. It is only too easy for the busy executive to fall into this trap and, partly as a result, he may become involved in the second factor, chain smoking, because smoking causes a rise in the blood sugar level. Unfortunately, excessive smoking sooner or later has the opposite effect, and relative hypoglycæmia again occurs. Finally the executive tends to finish the day with several drinks; on this Portis, Zitman and Lawrence, though they advise against alcohol, make little comment beyond referring to the resultant sense of well-being from removal of cortical inhibitory influences—an effect on whose virtue opinions will differ. In the "philosophical approach to the treatment of exhausted executives", as they describe it, Portis, Zitman and Lawrence advocate eradication of factors that have brought on or magnified the fatigue states, with dietary and pharmacological measures "to normalize the disturbed carbohydrate metabolism". These measures include administration of atropine and phenobarbital in suitable doses throughout the twenty-four hour period and an adequate diet, the details of which appear to follow generally accepted standards. Their treatment in general follows common-sense lines and commends itself whether or not the theories put forward on the ætiology of the exhaustion state are correct. The problem warrants the careful consideration of practitioners generally, and this presentation of it as, to some extent, an entity does a real service. Perhaps our young Australian executive does not always live at the pressure of his American counterpart, but a similar problem can and does arise at times. It could often perhaps be averted if, as is suggested in this paper, employers in industry insisted on periodic medical examinations for their executives.

[1] *The Journal of the American Medical Association*, December 2, 1950.

Abstracts from Medical Literature.

BACTERIOLOGY AND IMMUNOLOGY.

Serological Studies of Corynebacterium Diphtheriæ.

G. H. MINZEL AND V. J. FREEMAN (*The American Journal of Hygiene*, May, 1950) have investigated the use of a surface active agent in the preparation of uniform suspensions of *Corynebacterium diphtheriæ* for serological typing. Cultures were grown in 5% strength serum broth, and subcultures in broth containing 0·7% of "Tween 80". After incubation the cultures were centrifuged and the deposit was suspended in 1·0 millilitre of the culture fluid for slide agglutination, or in 1·5% sodium chloride solution for tube agglutination. Antisera were prepared by the intravenous injection of rabbits with formalinized cultures over two periods of three weeks. A comparison of bacterial suspensions as prepared by various workers established those prepared with the addition of "Tween 80" as most uniform. Then a comparison of agglutination titre of diffusely growing strains without the addition of "Tween", and after growth in the "Tween" medium, was made. The reduction of titre in the results of emulsions prepared from "Tween 80" cultures was never more than one dilution.

THE same authors studied the antigenic relationship between small colony types of *Corynebacterium diphtheriæ* and *Corynebacterium diphtheriæ*-like bacilli as determined by the method of slide agglutination. One group of virulent strains was isolated from patients and contacts in Grays Harbour; these resembled *intermedius* strains. Some atypical strains caused slow fermentation of glucose and varying fermentation of sucrose. Another group of atypical strains were non-toxigenic. It was shown that the Grays Harbour strains were of a single group, and that *intermedius* strains from Canada and Australia also belonged to this group. The atypical strains could be differentiated serologically from them, thus demonstrating the usefulness of the slide agglutination technique.

Somatic Antigens from Bacterium Coli.

LILA HAYES AND N. F. STANLEY (*The Australian Journal of Experimental Biology and Medical Science*, March, 1950) have studied the preparation and properties of somatic antigens isolated from *Bacterium coli*. The antigen was contained in the polysaccharide fraction of the organisms, which was obtained by one of two methods, either by grinding the bacterial bodies or by lysing them with glycine; the ultimate white powders obtained by these two methods showed differences in the traces of protein and in phenolic substances. Immune sera were prepared in rabbits, in one case by the use of heat-killed organisms and in one by the injection of polysaccharide. The intravenous injection of the substances into normal rabbits produced leucopenia, a rise in the level of blood sugar and lactic acid over five hours, then a steady increase in the number of leucocytes and a fall in the level of blood sugar and lactic acid. The leucocytes were susceptible to lysis by the polysaccharide. In the test tube the immune sera produced a precipitin ring with high dilutions of the polysaccharide antigen. A modification of the technique for coating red cells with the polysaccharide was developed, and the immune rabbit sera were tested. They agglutinated specifically the coated red cells in high dilutions of serum. The authors describe in detail the differences exhibited by the two fractions of polysaccharide antigen isolated from *Bacterium coli*.

Hawaiian Strain of Dengue Virus.

R. W. SCHLESINGER (*The American Journal of Hygiene*, March, 1950) has observed the propagation in chick embryos of the Hawaiian strain of dengue virus. He records sustained serial passage in eggs after 10 intracerebral passages in mice; this had not been achieved before the strain had become mouse-adapted. After 38 passages through eggs, opportunity was taken to inoculate egg material into two human patients suffering from nephrosis. This was done because such patients have been known to exhibit striking improvement after an attack of virus disease such as measles. The inoculations were made subcutaneously. One patient showed no clinical signs, but the other had a rash and fever on the ninth and tenth days after inoculation. Attempts to isolate virus from the patients failed, but in both cases the serum developed protective antibodies against infective virus in eggs. No complement-fixing antibodies could be demonstrated.

Cytoplasmic Bodies from Lymphocytes.

R. WILLIAMSON (*The Journal of Pathology and Bacteriology*, January, 1950) has studied the production of cytoplasmic bodies by lymphocytes. He used lymph nodes from normal rabbits and made impression preparations rapidly after the death of the animal, fixed them in Helley's fluid and applied various staining methods. The pseudopodia of lymphocytes, so rarely seen in films from peripheral blood, were frequently visible, and small cytoplasmic bodies, in which mitochondria were present, could be demonstrated. The author discusses the possibility that this is the mechanism by which large lymphocytes become small, and also that it may be a means by which the γ globulin is distributed throughout the body.

Studies on Tubercle Bacilli.

HUBERT BLOCH (*The Journal of Experimental Medicine*, December, 1950) has continued his studies on tubercle bacilli by establishing a relationship between the physiological state of the organisms and their pathogenicity. He used very young cultures and aged cultures, growing them for three days or three weeks in Dubos "Tween 80" medium, and infecting groups of mice by intravenous injection of 0·1 millilitre of bacillary suspensions. Among mice infected with aged cultures, the survival time varied up to ninety days, and the animals developed large lung lesions with mediastinal glandular enlargement and scanty lesions in other organs. The microscopic appearances were those of acute inflammation; giant and epithelioid cells were rare. After inoculation with young cultures, the predominating lesion was in the heart, consisting of multiple small abscesses with enormous numbers of bacilli. Very minute lesions were present in other organs. These appearances were similar to those produced by Yersin with avian cultures in rabbits. The author showed that by the use of very young cultures, this Yersin type could be produced by both bovine and human strains of tubercle bacilli. He related the type of lesion produced to the amount of cord factor present, an object towards which earlier experiments had been directed; the cord factor is a product soluble in petroleum ether which is concerned in the metabolism of the bacilli.

A Viral Agent from Non-Paralytic Poliomyelitis Pathogenic for Suckling Mice.

F. SARGENT CHEEVER, JOAN B. DANIELS AND E. FREEMAN HERSEY (*The Journal of Experimental Medicine*, August, 1950) have studied a viral agent isolated from a case of "non-paralytic poliomyelitis" and pathogenic for suckling mice, with its possible relation to the Coxsackie group of viruses. They state that it was isolated from the fæces of a patient treated during September, 1949, for a mild illness from which she recovered completely. Three samples of the patient's blood were also secured for study. The inoculum from the stool was treated with penicillin and streptomycin, and mice not more than forty-eight hours old were inoculated intraperitoneally; it produced lesions in heart muscle and fat, degenerative changes in the brain, parenteritis and death. The incubation period in the suckling mouse was six days, but after passage, it became stable at two to three days; the mice usually died after forty-eight hours. It was found that virus could be isolated from the ground carcass as easily as from the brain tissue, and also from isolated samples of adipose tissue. Attempts to infect monkeys, fertile eggs and guinea-pigs failed, but infant voles may be susceptible. Neutralization tests, in which a mixture of serum dilution and virus suspension is injected into suckling mice, showed that the patient from whom the virus was isolated possessed antibodies against her own agent. The antibody could also be demonstrated in normal adult serum, and in some specimens of serum from some cases of epidemic pleurodynia. No clear-cut evidence of serological relationship could be obtained with the Coxsackie group of viruses.

Lesions Caused by Viruses from Non-Paralytic Poliomyelitis and Pleurodynia.

ALWIN M. PAPPENHEIMER, JOAN B. DANIELS, F. S. CHEEVER AND T. H. WELLER (*The Journal of Experimental Medicine*, August, 1950) describe lesions caused in suckling mice by certain viruses isolated from cases of so-called non-paralytic poliomyelitis and of pleurodynia. They state that in the heart of mice dead of the Powers virus necrosis of heart muscle and calcification occurred; coagulative necrosis of fat cells was conspicuous, as also was pancreatitis. When this last occurred, the survival time of the mice was very short. Degenerative changes occurred early in the central

nervous system, with ultimately a fully developed state of meningo-encephalitis. The lesions vary with the age of the inoculated mice, pancreatitis and myocardial necrosis occurring only in animals less than six days old at inoculation. Two strains of pleurodynia virus appear to attack the liver primarily, producing diffuse hepatitis, with varying amounts of fat necrosis pancreatitis and central nervous system involvement, not unlike those of Powers virus. The myositis which is described as characteristic of the Coxsackie group of viruses does not appear constantly within that group, and it may occur in suckling mice infected with other types of virus.

HYGIENE.

Health Hazards in the Manufacture of Alkaline Accumulators.

LARS FRIBERG (*Acta medica Scandinavica, Supplementum* 240, accompanies Volume CXXXVIII, 1950) reports a clinical and experimental study into health hazards associated with the manufacture of alkaline accumulators. He describes an occupational disease, the essential symptoms of which have hitherto been unknown. He found that the workers in an alkaline accumulator industry were exposed to both cadmium iron dust and nickel graphite dust. In 95% of the cadmium dust and in 85% of the nickel graphite dust particles were found of a size less than 5μ. The main changes revealed by clinical examination of 58 male workers exposed to the dust in question were pulmonary emphysema, proteinuria, an increase of the sedimentation rate, some degree of liver and kidney injury, anosmia and certain dental changes. They complained of tiredness, shortness of breath, cough and impaired olfactory sense, with reduced physical working capacity. The method of examination of workers of similar factories abroad has confirmed these findings. Further light has been thrown on them by animal experiments, and the author considers that the changes appearing in the workers must be considered to be due to exposure to cadmium dust. Exposure to other dusts, especially nickel, may have contributed in some measure to the pulmonary emphysema. The ætiology of the anosmia is not certain. The author found no symptoms of poisoning in workers with a short period of employment (one to four years); chronic cadmium poisoning appears to make its first appearance relatively late. The prognosis seems to be poor. The author considers that the limit value at present accepted for the maximum allowable concentration of cadmium should provide a satisfactory margin of safety.

Quartz in Industrial Dusts.

L. SCHMELZER (*A.M.A. Archives of Industrial Hygiene and Occupational Medicine*, February, 1951) describes a rapid method for determining quartz content in industrial dusts by X-ray diffraction. The average absolute accuracy of the method was found to be ±5% of the amount present, but in the ranges below 10% of quartz, errors as high as 50% were found. The method was found to have considerably greater accuracy and reproducibility than the chemical methods in use. Very substantial savings of time were found in it, as compared with the chemical methods and with the photographic or internal-standard X-ray methods. The requirement of expensive instrumentation appeared to be the only limiting factor in the general application of the techniques. Methods for determining quartz content in industrial dusts have received much attention, and all the techniques of analytical chemistry and of mineralogy have been used, but all methods have some shortcomings that limit their usefulness.

Survival of Enteric Organisms in Soil.

W. L. MALLMANN AND W. LITSKY (*American Journal of Public Health and The Nation's Health*, January, 1951) draw attention to the discharge of sewage in increasingly large volumes into streams and rivers. They suggest that in areas where water from these polluted rivers and streams is used to irrigate vegetable gardens the resulting vegetables may carry enteric disease organisms. Experiments were carried out to find an indicator organism in sewage-contaminated waters that would be of value in measuring the health hazards associated with irrigation water. The isolation of pathogenic organisms was sporadic, but the fact that pathogens such as *Salmonella typhosa* were isolated emphasizes the need for the control of such contaminated waters if they are used to irrigate vegetables. Virulent strains of *Salmonella typhosa* used experimentally in contact with soil did not lose the Vi antigen, and they survived for varying periods up to nineteen days. The only organisms, other than the coliform organisms, found in sewage that could be used as indicators of fæcal contamination were the enterococci. Coliform organisms were found to persist in soil for long periods. Enterococci were found to die out rapidly in the soil. Virulent typhoid bacilli died out in soil much more rapidly than did the enterococci. The longevity of the coliform organisms, the typhoid bacilli, and the enterococci in soil was prolonged with an increase in the organic content of the soil. The authors concluded that enterococci would appear to be good indicators of public health hazard from sewage in soils and on vegetables.

The Use of Milk.

E. PHIPARD (*American Journal of Public Health and The Nation's Health*, January, 1951) has investigated the effects of a number of factors on the use of milk as a food in the United States of America. He states that the present-day annual consumption is 250 quarts per person. This is less than in 1945-1946, but more than it was in 1942. A study of the diets of a cross-section of urban families has revealed that families in the higher income group eat more cream, ice-cream, cheese and fluid milk and less dried milk and buttermilk than those in the lower income groups. A variation occurs in the milk diet of families in similar income groups in different cities. A study of the diets of individual families and of the diets of individuals in those families in both country and city shows wide differences in the amount of milk and milk products consumed. A recent survey of 4000 school children in New York State revealed that 16% of boys and 23% of girls had less than a pint of milk per day, and one-day food-intake surveys showed that 11% of pregnant women, 34% of men workers and 41% of women workers consumed either no milk or less than half a cup of milk per day. In a group of 700 pregnant women, 39% drank less than half a pint of milk per day. The author considers that milk is the most economical source of calcium. It has been shown that milk products, less butter, cost one-fifth of the cost of the total diet, but they provide two-thirds of the calcium, half the riboflavin and one-fourth of the protein, in addition to other valuable nutrients in that diet. The author suggests that the consumption of milk could be increased by adding skimmed milk to bread and by educating the public in the use of the cheaper forms of milk products as a source of valuable nutrients.

The Effects of So-Called Inert Dusts.

A. J. VORWALD (*Archives of Industrial Hygiene and Occupational Medicine*, August, 1950) discusses inert dusts in air pollution. He states that these may have a nuisance value. They may damage property. They may interfere with the bacteriostatic and bactericidal effect of sun rays. Particulate dust may be inhaled. Some may remain in the lungs and give rise to pneumonokoniosis. If the inhaled dust is active, significant pulmonary change may occur accompanied by dysfunction and susceptibility to infection. Even an inert dust may produce pulmonary change or interfere with function, depending on its physical and chemical character, its concentration in the air, the temperature and humidity of the air, the amount of dust inhaled and retained, the duration of exposure, and finally the state of the respiratory tract. Spherical particles of quartz larger than 3μ do not cause tissue damage. Smaller particles of silicon dioxide produce the inflammatory reaction of nodular silicosis, but particles of this substance less than 0·1μ cause a diffuse cellular inflammatory reaction. During an industrial process an inert substance may be changed to a substance whose air-borne particles are active and capable of producing an inflammatory reaction. Inert particles may carry a gas, an allergen, a biological agent or any other contaminant capable of damaging pulmonary tissue. Inert particles embedded in the lung tissue may adsorb and concentrate an irritating agent liberated by an infecting organism already in the body tissues. Massive fibrotic lesions in tuberculo-silicotic lungs may be due to adsorption of tuberculin onto particles of inert carbon or of iron oxide. Inert particles may cause active particles in air containing a mixture of particulate substances to agglutinate into large inert clumps, or they may form a covering for the active particles and thereby reduce their toxic action. The author describes the macroscopic and microscopic changes that occur in the lung after inhalation of an inert dust. The main feature of these changes is the absence of the inflammatory reaction which results from the inhalation of an active dust. The author concludes that the action of an inert dust can be determined only after careful clinical and experimental studies.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal Alexandra Hospital for Children, Camperdown, on April 18, 1951. The meeting took the form of a series of clinical demonstrations by members of the honorary medical and surgical staffs of the hospital. Part of this report appeared in the issue of May 26, 1951.

Communicating Hydrocephalus Treated by Uretero-Dural Anastomosis.

DR. T. Y. NELSON and DR. M. SOFER SCHREIBER presented a review of 19 cases of communicating hydrocephalus treated by uretero-dural anastomosis. It was pointed out that prior to that operation the most popular procedure in the treatment of the condition was removal of the chorioid plexus from each lateral ventricle in order to diminish the production of cerebro-spinal fluid. The results of that operation were satisfactory only in patients in whom cerebro-spinal fluid resorption was impaired to a minor degree. In order to shunt the cerebro-spinal fluid from the lumbar subarachnoid space to the excretory pathway provided by the ureter, Heile in 1925 first carried out uretero-dural anastomosis after unilateral nephrectomy. The operation proved unsuccessful, largely because of the post-operative complications of retrograde infection travelling from the bladder to the subarachnoid space by way of the lymphatics in the wall of the ureter, or because of arachnoid adhesions which occluded the junction of the anastomosis. Matson, in *The Journal of Neurosurgery* of May, 1949, described a new method of performing uretero-dural anastomosis. Unilateral nephrectomy was performed through a flank incision. The incision being left open, laminectomy was carried out on the second and third lumbar vertebræ, the dura was opened in the mid-line and the arachnoid was punctured, and a polyethylene plastic tube was introduced and directed downwards to lie among the cords of the *cauda equina*. The dura was closed securely about the tube. The other end of the tube was tunnelled through the back muscles to the perinephric space and introduced into the ureter. The margins of the upper end of the ureter were then sutured securely to the fascia of the psoas muscle. Matson considered that the interpolation of a loop of polythene tubing between the ureter and the subarachnoid space obviated the possibility of retrograde lymphatic infection, and that the possibility that arachnoid adhesions might occlude the junction of the anastomosis was counteracted by the placing of the plastic tube well into the lumbar subarachnoid space and well away from the point of operative interference with the arachnoid. Matson also suggested that hydrocephalic infants subjected to the procedure should receive an extra two or three grammes of salt per day to counteract excessive chloride loss in the urine.

Dr. Nelson and Dr. Sofer Schreiber then gave details of the six cases in their series in which relief had been obtained. The first patient had been operated on on April 4, 1950, at the age of seven months, and two months after failure to respond to removal of the right chorioid plexus; the condition was of obscure ætiology. The hydrocephalus was arrested, and the patient was progressing favourably in March, 1951. In the second case the condition was due to a cerebral birth injury. The child was submitted to operation on June 21, 1950, at the age of ten months; the head circumference was 18·5 inches. On February 12, 1951, the child was well and the head circumference was 18·5 inches. In the third case the condition was of obscure ætiology. The child was operated on on August 18, 1950, at the age of one year and ten months. The condition was good on February 26, 1951. The fourth patient was operated on on September 27, 1950, at the age of six months. The head circumference was then twenty and one-eighth inches; on February 13 the head circumference was 20 inches. In that case also the ætiology of the condition was obscure. The fifth patient had a large tense sacral meningocele with hydrocephalus due to an Arnold-Chiari malformation which a posterior decompression at the age of ten months had failed to relieve. On October 20, 1950, at the age of twelve months, the sacral meningocele was excised and a uretero-dural anastomosis was performed. On January 21, 1951, the hydrocephalus was found to be relieved and the sacral meningocele cured. In the sixth case the condition was of obscure ætiology. The child was operated on on January 31, 1951, at the age of three months, the head circumference being twenty and a quarter inches. On March 5 the head circumference was nineteen and three-quarter inches.

Dr. Nelson and Dr. Sofer Schreiber then referred to the nine deaths that had occurred in the series, pointing out that six deaths were due to dehydration, the result of excessive loss of cerebro-spinal fluid in the urine. The oldest of the nine patients was aged seven months. They considered it evident that the death rate was greatest among younger patients, and that more operations were successful on older patients. Finally they showed and discussed a number of pathological specimens.

Recto-Vaginal Fistula and Subsequent Megacolon.

Dr. Nelson then showed a female child, who had been born with a high recto-vaginal fistula. An artificial anus had been made when she was aged eight days; this had functioned satisfactorily, but the child had little control. In July, 1949, cystoscopic examinations showed the fistula to be high up on the posterior vaginal wall. Excretion pyelography revealed no delay in excretion, but the bladder was pushed over to the right. X-ray examination after a barium enema showed that that was due to the development of a large megacolon due to the obstruction at the outlet. In September, 1949, a transverse colostomy was established, and had continued to function satisfactorily. In August, 1950, X-ray studies showed that the colon had returned to normal calibre. Dr. Nelson remarked that the child's present condition seemed the most satisfactory permanent state for her, as the prospect of obtaining a functioning anus was very poor. The vaginal fistula would be repaired at a later date.

Sacro-Coccygeal Tumour.

DR. J. STEIGRAD discussed two cases of sacro-coccygeal tumour. These will be reported in full in a later issue of the journal.

Hare-Lip, Cleft Palate and Congenital Anomalies of the Fingers.

Dr. Steigrad then showed a boy, who had been first admitted to hospital on August 3, 1946, at the age of two weeks, with bilateral hare-lip and cleft palate, bossing of the forehead, syndactyly of the middle three fingers of the right hand, maldeveloped left little finger, and syndactyly of the right and left first three toes. On December 16, 1946, an X-ray examination of the skull revealed dysostosis of the frontal bone, and no intracranial calcification. On December 19 operative reconstruction of the upper lip was undertaken. The vomer was split and the premaxilla pushed into line. Flaps were taken from the upper lip to the cleft. The premaxilla was wired in place. On January 17, 1947, the wire was removed, and on March 11 the patient was discharged from hospital.

He was readmitted to hospital on April 14, 1948. There remained the upper part of a cleft originally extending from the inner canthus of the left eye to the lip, and now extending as far as the left *ala nasæ*. A complete cleft palate with wide separation was present. In the right hand there was fusion of the skin of the conjoining sides of the lateral three fingers; the terminal phalanx of each appeared to be absent. There was a central rudimentary phalanx on the tip of the fused fingers. In the left hand there was a band of constriction across the first phalanx of the ring finger. The middle phalanx of the little finger was missing, and the terminal phalanx was rudimentary. In the right foot the terminal phalanges of the great and second toes were absent, and the three medial toes were fused at their bases. In the left foot the terminal phalanges of the medial three toes were absent, and the toes were fused along their whole length.

On April 15 a plastic operation was performed on the second web space of the right hand and split skin grafts were applied; the tissues uniting the index to the middle finger were divided. The child was readmitted to hospital on October 11, and on October 14 a further operation was performed on the right hand; flaps were formed on the anterior and posterior surface of the hand, the third and fourth fingers were separated, and a graft was taken from the thigh and placed on the cut surfaces.

At operation on April 20, 1949, the adjacent edges of the *ala nasæ* and the cheek were freshened; two layers of sutures were inserted. The operation field was distal to the lachrymal apparatus.

On October 12, 1949, the child was readmitted to hospital. He had been having convulsive seizures, starting on the left side of the face, moving to the arm and leg, and passing off in that order; unconsciousness had lasted for ten minutes. He had four seizures in all from the age of two years till the age of three years and three months. On

October 20 a plastic operation was performed on the left side of the nose. On November 1 a partial "take" only had been obtained at the apex of the cleft.

On February 20 the child was readmitted to hospital for two reparative operations on the palate. He was readmitted to hospital again on March 26, 1951, and on March 29 a repair to the palate was performed. A small residual hole was present at the completion of the operation. On April 12 the sutures were removed.

Hydatid Disease of the Liver.

Dr. Steigrad then showed a female child, who had been admitted to hospital on March 6, 1951, at the age of three years. The child's abdomen had been gradually increasing in size for twelve months prior to her admission to hospital, and during that period she had suffered from intermittent abdominal pain associated with some vomiting. The attacks were usually associated with fever and were attributed to tonsillitis or otitis. During her life the child had suffered from tonsillitis, otitis, conjunctivitis and hives. She had been born normally, and was the second child of the family. Her father was a drover and suffered from asthma. The child had lived in the Goulburn district all her life. She was said to dislike dogs, although they had often been present around the house.

On examination, the child was seen to be thin and pale, and to have a protuberant abdomen. The liver was palpable and grossly enlarged to about the level of the umbilicus in the mid-clavicular line. The left lobe of the liver was also palpable. Otherwise no abnormality was detected in the abdomen. A blood count gave the following information: the erythrocytes numbered 4,700,000 per cubic millimetre and the hæmoglobin value was 12·0 grammes *per centum*; the leucocytes numbered 16,000 per cubic millimetre, 53% being neutrophile cells, 38% lymphocytes, 2% monocytes, 6% eosinophile cells and 1% basophile cells. X-ray examination revealed gross enlargement of the liver, and the right hemidiaphragm was elevated. The lung fields appeared clear. The serum protein content was 6·5 milligrammes per 100 millilitres; the albumin content was 4·1 and the globulin content 2·1 milligrammes per 100 millilitres; the albumin-globulin ratio was 1:7; the figures were normal. The thymol turbidity test produced a value of 1·5 units, the cephalin flocculation test result was negative, the result of the Casoni test was positive, and the Wassermann and Mantoux tests both produced negative results.

On March 22 the abdomen was opened with a right paramedian incision, which was extended up to the costal margin. A large cyst was found under the right dome of the diaphragm. It was packed off as far as possible, some of the fluid was aspirated, and the fluid was replaced with formalin. The cyst was then opened and the fluid aspirated. The cyst wall was removed and some saline was introduced into the cyst cavity, which was then closed. A second cyst was located on the posterior aspect of the inferior surface of the liver; it was similarly dealt with. Both cysts were simple in nature. After operation the child was given penicillin and "Benadryl" prophylactically, and made an uneventful recovery.

On April 2 an X-ray examination revealed that the right dome of the diaphragm was still elevated to about the same extent as previously, but the lower border of the liver lay about 1·5 inches higher. A full blood count gave the following information: the hæmoglobin value was 13·9 grammes *per centum*, and the leucocytes numbered 19,000 per cubic millimetre, 47% being neutrophile cells, 28% lymphocytes, 3% monocytes and 22% eosinophile cells.

Acute Osteomyelitis, Pericarditis, Myocarditis and Venous Thrombosis.

DR. DAVID DEY presented a girl, aged eight years, who had been quite well in every way until January 24, 1951, when she developed an apparently causeless limp affecting the right leg. That night she had some fever, but by morning was better. An examination of her leg, particularly her knee, showed nothing significant. Between that time and her admission to hospital her symptoms varied, consisting mainly of fever and pain in the region of the right knee, but they were, on the whole, progressive. The physical signs were not striking, and the child was regarded as suffering from rheumatic fever, though osteomyelitis was considered. She had always been difficult and her condition was hard to assess accurately. On January 29, she became seriously ill with high fever, delirium, and swelling of the whole of the right leg. She also had abdominal pain and was admitted to hospital in a grave state. She was found to be extremely ill, irritable and delirious, with peripheral circulatory collapse associated with cold, patchy cyanosis and sweating. She had considerable pyrexia. The whole of the right thigh was very swollen with a lesser swelling of the lower part of the right leg and the right foot. The thigh was firm with very noticeable superficial veins. No localized tenderness could be found; all movements were resented, this appearing to be greater on movement of the hip than of the knee. There was abdominal tenderness of mild to moderate degree, generalized but possibly a little greater in the right iliac fossa. There was no other significant finding. Treatment was instituted with blood transfusion and subsequently continuous intravenous infusion to supply her requirements, massive doses of penicillin, and sedatives. Blood culture produced a growth of *Staphylococcus aureus* that was coagulase-positive and sensitive to all antibiotics. A blood count revealed a mild degree of anæmia and a total of 8000 leucocytes per cubic millimetre with no change in the proportions and some toxic changes in the granulocytes. X-ray examination of the right hip, thigh and knee showed no bony involvement. Next day her condition was little better. There was a pericardial friction rub present, which was easily palpable in the precordium. The spleen was palpable. There was still no definite localization of signs in her thigh. She was examined by an honorary physician, Dr. W. P. MacCallum, in consultation, and given "Chloromycetin" in addition to the penicillin. After this she developed a pericardial effusion, and the rub became impalpable. Her apex beat was palpable in the sixth intercostal space outside the nipple line. As she did not appear to show any response, aureomycin was substituted for the "Chloromycetin" on February 1. She developed scattered crepitations over her lung fields. On February 5 she began to show an improvement, this, curiously enough, following the exhibition of salicylates, which had been given more or less in desperation. From then on her general condition steadily improved and caused no further anxiety. The aureomycin therapy was suspended on February 17, and the penicillin therapy on March 13. Radiological examination of her chest on February 5 had shown gross cardiac enlargement and patches of bronchopneumonia, and for the first time a small amount of bone absorption was apparent in the metatarsus of the lower end of the femur on the medial side. Subsequent serial X-ray pictures showed progression of this to the typical appearances of acute hæmatogenous osteomyelitis, but clinically there was never any very good evidence to localize the disease until a late stage. The lung opacities resolved, and the size of the heart diminished. On February 26 a radiographic diagnosis was made of osteomyelitis of the lateral third of the right clavicle, but related signs or symptoms were lacking even in retrospect. An electrocardiogram on March 3 showed sinus tachycardia, a broad *P* wave and an increased *P-R* interval; the *T* waves were flattened and inverted in all leads, and the changes were regarded as consistent with myocarditis or pericarditis. The local condition of the leg showed as its striking features, at all times from an early stage, gross swelling and prominence of the superficial veins of the thigh as well as of the lower part of the abdomen, with nothing very definite in the way of localizing signs. Tenderness appeared early, mainly over the upper adductor region. The exact diagnosis was always in some doubt until February 5, when radiographic evidence was obtained of the site of the lesion. The lower part of the leg and foot showed œdema only, and it was early felt that the only explanation of the condition was a complicating, deep venous thrombosis due to the infection. There was never any suggestion of abscess formation. The whole condition subsided slowly, but the veins remained prominent. Early treatment with heparin was felt to be dangerous in view of the patient's serious condition. It was intended to fit an elastic stocking before she was out of bed when convalescent from her myocarditis. The complete diagnosis was acute hæmatogenous osteomyelitis of the lower end of the right femur, secondary osteomyelitis of the lateral end of the clavicle, right femoral thrombophlebitis, and complicating myocarditis and pericarditis.

Œsophageal Surgery.

DR. E. H. GOULSTON showed three patients to illustrate various aspects of œsophageal surgery. The first patient had been suffering from congestive splenomegaly (Banti's disease), secondary to obstruction of the portal and splenic veins. The patient was a boy who, when first admitted to hospital in January, 1944, had been aged two years. The eleventh child in his family, he had been born after a normal pregnancy, but had failed to thrive for the first few months of life for no apparent reason. He had had attacks of hæmatemesis, with and without melæna, when aged nine months, twelve months, eighteen months, and

two years. (He had subsequent attacks of hæmatemesis when aged two and a half years, three and a half years and four years.) When examined at the time of his first admission to hospital, he had light brown, pigmented spots on the trunk, which subsequently became darker. The liver and spleen were not palpable at the time, but they subsequently became palpable. Findings from the full blood count were consistent with effects of blood loss only. The thrombocytes numbered 200,000 per cubic millimetre. The bleeding time was a quarter of a minute, and the coagulation time four minutes. X-ray examination after administration of a barium meal revealed no abnormality, and the long bones and skull were radiographically normal. Sternal biopsy revealed normoblastic hyperplasia but no Gaucher cells. Eventually, after repeated admission to hospital and blood transfusions, splenectomy with ligation of dilated œsophageal veins was carried out on May 21, 1946. The spleen was found to be affected with "splenic fibrosis" consistent with Banti's syndrome with many adhesions. The child was well for almost twelve months, but hæmatemesis again occurred in April and August, 1947 (following fracture of the right and left clavicle, respectively), in November, 1947, in May and July, 1948, and in March and September, 1949. The prothrombin time determined in July, August and September, 1948, respectively, was five minutes, thirty seconds and twenty seconds as against control values of fifty seconds, thirty seconds and twenty-three seconds. Other values obtained in July, 1948, and September, 1949, respectively, were as follows: serum bilirubin content, 0·3 milligramme per 100 millilitres and nil; serum protein content, 7·1 and 6·3 grammes per 100 millilitres; serum albumin content, 4·8 and 4·5 grammes per 100 millilitres; serum globulin content, 2·3 and 1·8 grammes per 100 millilitres; albumin-globulin ratio, 2·1 : 1·0 and 2·5 : 1·0. After X-ray examination with swallowing of a barium bolus in September, 1949, the radiologist reported that the outline of the lower part of the œsophagus suggested the presence of œsophageal varices. A thymol turbidity test produced a value of less than one unit, and the result of a cephalin flocculation test was negative. In March, 1950, the child had a further hæmatemesis and was very ill for five weeks with swinging pyrexia, hæmatemesis and melæna. Blood and penicillin were administered, and when his condition was satisfactory œsophago-gastrectomy was performed. The findings at operation were omental adhesions to the stomach and old scar, very vascular adhesions to the lower part of the diaphragm and the anterior abdominal wall, and large œsophago-cardial varices. The liver was of normal size and had no apparent fibrosis. The upper half of the stomach and a half-inch of œsophagus were removed. The child had a stormy convalescence with atelectasis of the left lung and subphrenic abscess, but was finally discharged from hospital in November, 1950, after having been well for three months. He was readmitted to hospital in March, 1951, with a diagnosis of left lobar pneumonia, but apart from that, had been quite well and had been free from hæmatemesis.

The second patient, a girl, had been admitted to hospital in January, 1951, at the age of three days. She was the eighth child of her family, having been born after a normal pregnancy and quick labour, complicated only by breech presentation and hydramnios. It was stated that she could not swallow and regurgitated tube feedings through the nose, but there was no cyanosis with the feedings. She had passed meconium and urine. She was found to be a small baby with a moderate degree of jaundice and only fair hydration. The fontanelle was slightly depressed. An anal opening was present at the lower end of the posterior wall of the vagina. X-ray examination of the chest after instillation of lipiodol showed a blind upper end of the œsophagus with a "spill-over" of opaque material into the lungs. At operation on the following day, it was found that the upper part of the œsophagus ended blindly at the level of the first thoracic vertebra and the lower part of the œsophagus ended blindly at the level of the second and third thoracic vertebræ. A fistula was present between the lower part of the œsophagus and the trachea. Through a posterior approach the fistula was located and end-to-end anastomosis of the œsophagus carried out over a tube which was later removed. Towards the end of the operation, which took one hundred and thirty minutes, the child stopped breathing for five minutes, but responded to resuscitative measures. Blood transfusion was given throughout the operation, and the baby was nursed in a steam tent for the first twenty-four hours after operation. During convalescence blood transfusions and intravenous fluid therapy were required. Oral feeding was commenced ninety-six hours after operation. Progress during convalescence was fluctuating, but at the time of the meeting the baby was in her twelfth post-operative week and was doing well.

The third patient was a girl who had swallowed caustic soda at the age of seven years and had become unable to swallow anything except occasionally fluids. Gastrostomy had been carried out, and feeding by that route had continued for ten years. In February, 1950, exploration was carried out through a thoraco-abdominal approach, and œsophago-gastrectomy was performed. The middle and lower thirds of the œsophagus were removed, and the stomach was brought up through the diaphragm and anastomosed to the œsophagus above the aortic arch. The gastrostomy opening was left. The patient was then able to swallow. Later she had some difficulty in swallowing, and after œsophagoscopy the diaphragmatic opening was dilated. She still had some difficulty in swallowing, and X-ray examination with the swallowing of a barium bolus revealed a stricture of the stomach at the level of the diaphragm. Examination with an œsophagoscope through the gastrostomy opening showed gastritis and slough in the stomach. The patient was discharged from hospital for three weeks, during which time she fed herself through the gastrostomy opening. Then the stricture was dilated from above and below. Communication was established, and a catheter was inserted on a loop of thread. Swallowing became possible. A larger bore catheter was later used to replace the first. The patient became able to take liquids, then semisolids, and finally solids by the mouth. Further dilatation was necessary at intervals up to the end of 1950. In March, 1951, she reported to the out-patient department, having been well for three months. The gastrostomy tube was removed, and at the time of the meeting she was swallowing all foods.

(To be continued.)

Correspondence.

SOME POINTS IN THE MANAGEMENT OF VARICOSE VEINS.

SIR: Dr. C. H. Wickham Lawes's article appearing in THE MEDICAL JOURNAL OF AUSTRALIA on May 5, 1951, may stimulate some interest in the treatment of varicose veins. It would be instructive to know from his 1000 operations how long the average operation takes, anæsthetic used, days in hospital and average time off work; whether he has had any of the complications that he describes.

Retrograde injection could produce all the complications mentioned and may be safe with an experienced operator, but is not suitable for general use.

After observing the results of treatment in Australia and seeing surgeons in Britain operating on varicose veins last year, one is struck by the lack of interest in the whole subject and by the high percentage of failures from all forms of treatment.

After carefully observing and treating many cases of varicose veins for eight years by a minimum of surgery and a maximum of controlled injections and bandaging, it is possible for the worst cases to be cured in five visits with little or no loss of work and a relapse rate of less than 5% in three years.

Yours, etc.,

J. N. R. STEPHEN.

Newcastle,
May 8, 1951.

THE ARTHUR WILSON MEMORIAL FUND.

SIR: The Arthur Wilson Memorial Fund is to be devoted to research into childbirth problems. Donations may be sent to Dr. C. K. Churches, Honorary Treasurer, 122 Flinders Street, Melbourne, C.1, and will be acknowledged in this journal.

Yours, etc.,

C. K. CHURCHES.

122 Flinders Street,
Melbourne, C.1,
May 10, 1951.

The following donations have been received and are acknowledged with thanks: previously acknowledged £1238 5s., Dr. A. E. Rowden-White £100, Dr. Ella Macknight £100, Dr. W. D. Saltau £100, Dr. K. McLean £31 10s., Dr. W. R. Griffiths £21, Dr. James Smibert £21, Dr. H. Ian Jones £15, Dr. L. W. Johnston £10 10s., Dr. and Mrs. Russell Sherwin £10 10s., Dr. Irving Buzzard £10 10s., Dr. H. R.

Millikan £10 10s., Sir Hugh Devine £10 10s., Dr. Archie S. Anderson £10 10s., Dr. James H. Paterson £10 10s., Dr. and Mrs. Max Rees £10 10s., Dr. Dulcie G. Rayment £10, Dr. and Mrs. J. Ringland Anderson £5 5s., Dr. A. C. Keane £5 5s., Dr. S. W. Williams £5 5s., Dr. J. R. Watt and Dr. Kathleen Inglis £5 5s., Dr. H. T. Beamish £5 5s., Dr. E. J. Grieve £5 5s., Dr. John P. Horgan £5 5s., Dr. I. M. King-Scott £5 5s., Dr. Colin Macdonald £5 5s., Dr. Geraldine C. Amies £5 5s., Dr. and Mrs. Sidney Plowman £5 5s., Dr. and Mrs. John O'Rorke £5 5s., Dr. B. R. Hallows £5 5s., Dr. T. W. Vorrath £5, Dr. A. Campbell £3 3s., Dr. Eric Gutteridge £2 2s., Dr. C. Hopkins £2 2s., Dr. K. L. Langlands £2 2s., Dr. K. Eager £2 2s., Dr. W. L. Colquhoun £2 2s., Dr. and Mrs. Maxwell Hoban £2 2s., Dr. M. Gillespie Jones £2 2s., Dr. J. B. Devine £2 2s., Dr. John A. Game £2 2s., Dr. J. Maxwell Casley £1 1s. Total: £1817 2s.

COXSACKIE VIRUSES IN SOUTH AUSTRALIA.

SIR: Under the ægis of the South Australian Advisory Committee on Poliomyelitis, a University Committee for Poliomyelitis Research is investigating cases, classed as atypical poliomyelitis or pleurodynia, for viruses of the Coxsackie group. So far a virus (designated P14) resembling the Coxsackie group has been obtained from infant mice inoculated with throat washings from a case (D.W.H.) of so-called pleurodynia.

Primary inoculation resulted in weakness and paralysis of the infant mice, followed by death on the sixth to ninth day. Subsequent passages of muscle of infected mice produced emaciation, weakness and paralysis in infant mice, which died on the third to the sixth day. Three-weeks-old mice inoculated with the same material remained unaffected.

Stanley and Hayes in *The Australian Journal of Science* for December, 1950, also recorded the isolation of viruses, pathogenic for infant mice, and possibly belonging to the Coxsackie group. Their three strains of virus came from cases of non-paralytic poliomyelitis in Sydney.

A detailed account of our investigation will be published elsewhere when further study of the virus is completed.

Yours, etc.,

Department of Bacteriology, University of Adelaide, May 16, 1951. NANCY ATKINSON.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held in the Anatomy Lecture Theatre, Frome Road, Adelaide, on May 4, 1951.

Rabbit Myxomatosis.

MR. E. W. LINES read a paper on the epidemiology of rabbit myxomatosis. Mr. Lines described briefly the epizootic of rabbit myxomatosis, which had spread from a primary focus near Corowa to south-west Queensland and to South Australia in a period of six weeks to two months. The disease had been released in September, 1950, and apparently died out, but reached epizootic density there in the first week in December. In six weeks it had reached Cunnamulla, Queensland, a distance of approximately 1000 miles. If the time for a generation of the disease was taken as ten days, even 200-mile jumps would mean an average progress of but 20 miles per day.

Mr. Lines said that the most prominent vector for the disease during the present epizootic in New South Wales had undoubtedly been the mosquito, but fleas and sand flies also contributed to the spread in some places. The most likely vehicle for the rapid spread in space was probably passive translation of infected mosquitoes in moving masses of air. Support for this thesis had been given by the practically simultaneous flare-up of the disease during the first week in February along the Murray river from Renmark to Mannum. Local experiments proved that mosquitoes were the vectors; for both the exposure of clean rabbits to mosquitoes in the epizootic area and the injection of pulped mosquitoes into rabbits induced the disease. Mosquitoes had been proved to remain infective with myxomatosis for up to fourteen days. However, a much longer infective life might be expected, for *Aëdes ægypti* had been proved to remain infective with yellow fever for fifty-seven days and could survive for one hundred to one hundred and fifty days after becoming infected. Thus mosquitoes carrying myxomatosis would remain infective long enough to be moved considerable distances by wind. The possibility that carrion-eating birds might deposit excreta containing infective virus at considerable distances away was also considered, but the route by which this would reinfect rabbits was not very clear. In those cases in which information was available, the transport of infected rabbits by farmers had failed to induce an effective local outbreak.

Obituary.

CHARLES ALFRED HOGG.

WE are indebted to Dr. Oliver Latham for the following account of the career of the late Dr. Charles Alfred Hogg.

Charles Alfred Hogg was a remarkable man. When fairly started, his life was one of unremitting action to its end. He spent his early school years at the Hutchins School in Hobart and at a school near Ross in Tasmania. Like many famous men, including William Stokes, he caused his relatives much anxiety during his school days and he woke one day to find himself in an insurance office as a clerk. A few hours' reflexion caused him to ask himself whether he was to spend the rest of his days as a jackaroo on an office stool at the beck and call of everybody. A chance was given him at the Launceston Grammar School and in

due course he came top of the examination for a State scholarship of £300 a year tenable for five years at any university. He chose Edinburgh and became a successful student. He obtained the junior prize in pathology, the senior prize going to the late Professor Arthur Welsh, sometime professor of pathology in the University of Sydney. Qualifying in due course with a gold medal, Hogg obtained a resident post at the Manchester Infirmary. He often quoted a passage from his lecturer in medicine or therapeutics: "a small dose of chromic acid would cure most cases of gastric ulcer." At Edinburgh he came into contact either at work or on the cricket field with many Australians who had a profound influence on his after life. This laid the foundation of his great capacity to approach any authority which he thought would advance the cause of his mental patients. It must not be supposed that in his student days he was passing rich on three hundred pounds a year. His widowed mother had seven children for whom she had to provide and she was always foremost in his mind; so it was that much of his prize money did not leave Tasmania. At this point reference may be made to the fact that at any hour of the day or night he was at the complete service of patient, relative or friend who needed immediate medical or surgical help; every other interest was subordinated to this.

When he returned to Australia, Hogg commenced his life's work as resident medical officer at Gladesville Mental Hospital. Here he had as his companions his superintendent, the late Eric Sinclair, E. Becks, a great lay administrator, and Frank Barton, Master in Lunacy. Dr. Manning was a frequent visitor. He was next moved to Parramatta and finally became senior medical officer at Kenmore Mental Hospital. Here he found his *métier*, for he spent many years there either as acting or as permanent medical superintendent. He was always a keen clinician and a skilled neurologist, and it was his constant endeavour to instil into his medical officers the importance of the full examination of the patient and also the application of all necessary biochemical investigations as an aid to diagnosis. His insistence on the importance of physical signs and symptoms and of their influence on and their interpretation by the psychotic, antedates the appearance of what has become known as psychosomatic medicine. He had for years stressed the claims of resident medical officers for a university course in psychiatry, and when the diploma course was established in 1923 he himself took the course with other students. He insisted that the lessons of pathology were still of importance in the realms of psychiatry, and it was therefore necessary for one of his medical officers to spend six months of his training in carrying out any pathological and biochemical work required by other medical officers in his department. To this end he founded a laboratory in the hospitals where this work could be performed. Many of his *confrères* will remember carrying out with him in the early hours of the morning examinations of blood and cerebro-spinal fluid when serious conditions such as *encephalitis lethargica* and so on were suspected. Always a prodigious worker, Hogg expected others to be the same. As Inspector-General it was his fortune to be in charge of the destinies of the Mental Hospitals Department for ten years which included the period of the depression. It was his proud boast that he obtained from the Government a sum of £100,000 a year for ten years and that he was able to develop a building programme for the department and to some extent to relieve the overcrowding which had been increasing through the years. To the duties of Inspector-General he brought his meticulous attention to detail, and when he paid official visits to the country hospitals particularly he spent three or four days of careful investigation. The completion of the main hospital at Orange and the erection of the female division and the completion of the remarkable admission blocks and criminal division at Morisset will remain monuments to his work. Funds were not always available for all that he required, and if the Minister was implacable one day, Hogg was sure to be on his doorstep the next and on following days until some results could be obtained. To him must go credit for the eventual establishment of psychiatric out-patient departments in general hospitals adjacent to large mental hospitals, and the clinics established by him at Orange, Newcastle and Kenmore still render valuable out-patient service to those in need of psychiatric treatment. The Department of Neuropsychiatry at the Royal Prince Alfred Hospital owes a great deal to his efforts, as does also the Buckland Convalescent Hospital at Springwood. When he retired from the office of Inspector-General he did not cease to take interest in, or to give service to, psychiatry. He had been for many years an active member of the Section of Neurology of the New South Wales Branch of the British Medical Association and in fact was a foundation member of the section. He believed that if psychiatrists were interested in general medicine then general practitioners would be interested in psychiatry. His last words embodied a wish for a larger proportion of practitioners to be cognizant of the mental needs of their patients. It was impossible for a man with such a nature to escape criticism, but his friends always felt that he was a fair fighter and he was certainly always ready for debates.

Hogg was a first-rate cricketer and he played regularly with his hospital team. Many a strong visiting team at Easter, at Whitsuntide or at Christmas found victory hard to obtain, for he would study the peculiarities and reputations of his visitors before they arrived and would take care to produce the necessary counter stroke. On one occasion his surprise packet for the visitors was none other than Arthur Mailey. He trained his two sons from their earliest childhood to play cricket; an old tree served as a wicket. He saw each of them represent the university team and play in inter-university matches; they also carried on the game when they were members of the Australian Army Medical Corps in the Australian Imperial Force. He was intensely loyal to Tasmania and kept in touch with her interests. He often spent his leave there; sometimes he did work as a *locum tenens* and went to endless trouble to visit hospitals and clinics to gain further experience in surgery, medicine and in neurology. Sometimes when he did not spend leave in Tasmania he would visit Sydney where he followed the late Sir Herbert Maitland in his surgical work. He was a keen sportsman and fisherman and he organized fishing parties for patients, taking them in lorries to the Abercrombie river.

No account of Charles Hogg would be complete that did not mention his wide circle of friends, his fight for the rights of the public service, and his loyalty to the principles and ethics of the British Medical Association. His flair for coming into contact with important people and interesting them in his hospital schemes did much to advance the welfare of his patients and the institutions under his care. To his junior medical officers and certain medical students and also "failed M.B.'s" he was more than a teacher—he was a paternal guardian. To perform and get through all that he undertook needed the ablest mind and the strongest constitution. In regard to the latter the writer remembers a trip to the steep slopes of the Nattai river region. While negotiating a sheep walk shored up by saplings, Hogg assisted his progress by springing from tree to tree. A broken branch caused him to crash and roll over and over like a Rugby football down the steep sides, missing rocks, logs and upright stumps by inches. All he said when he was rescued was: "The diagnosis is a stiff neck." In addition to the members of the medical profession at his funeral there was a large contingent of managers and clerks and stenographers—a striking witness to the friendship that always existed between them. He is survived by a widow, three daughters, and two sons, both of whom are members of the medical profession.

Dr. J. A. L. Wallace writes: Having succeeded Dr. C. A. Hogg when he retired from the office of inspector-general of mental hospitals, I was able to appreciate how much good work he had done for the hospitals, despite the perpetual difficulties in obtaining the finances to carry out any major improvements. Outstanding examples of his administration are the sanatorium for tuberculous patients at the mental hospital, Orange, and the new wards for criminal insane at Morisset, both completed just before he retired. Numerous other alterations and improvements bear testimony to his thoroughness and careful attention to detail. Any case he undertook to inquire into was carefully written up in essential particulars and covered every activity of the individual. After his retirement he was able to assist the Government as Official Visitor to Parramatta and Rydalmere Mental Hospitals and Mount St. Margaret and also until 1945 he was Court Visitor. His good work as a trustee of the Buckland Home at Springwood was evident in the original planning of the home and was greatly appreciated by the late Sir Thomas Buckland.

Dr. Eric Hilliard writes: My association with Charlie Hogg began some thirty years ago, when he was medical superintendent at Parramatta, and continued when he became our inspector-general and during the last ten years as official visitor. He was an extraordinarily well read man and eagerly perused magazines, journals or books having a bearing on medical subjects. But this was not all: he inquired into articles on buildings, farm work, social service aspects, physiotherapy, and occupational therapy. He had a keen eye for park-like surroundings and his designs for Orange included having the wards arranged far enough apart to do away with any barrack-like effect. He not only laid out the cricket grounds at Kenmore and Orange, but as his advice on cricket grounds was sought for far and wide, we often accompanied him fifteen to twenty miles out in the days of horse vehicles to lay out some distant village sports ground. He encouraged patients to secure psychiatrical treatment at ordinary hospitals and during his regime voluntary patients greatly increased in numbers. He also had his admission wards designated by law "reception houses" wherein patients not suitable as voluntary patients could be treated uncertified and given a chance to recover without certification. He certainly was responsible for the completion of a great building programme. He held every possible position in the Central Southern Medical Association at Goulburn. While allowing and encouraging his officers to assume every possible responsibility in their treatment of patients, he himself kept an amazing tag on everything that concerned his patients; his industry and energy in everything that concerned treatment were an unfailing encouragement and example to his staff.

Dr. H. H. Nowland writes: I first met Hogg in this wise: I had received a sudden call to Kenmore to relieve a stricken *confrère*. Instead of my arriving at Goulburn at 6 p.m., railway delays made it 1.30 a.m., and there at the station

to meet me was Charlie Hogg with horse and buggy; and more characteristically still, as soon as we reached Kenmore, he immediately took me on a night round to see a new system of night observation he had instituted for his epileptics. He also showed me the sweet and healthy state of over a hundred old and chronic dements who were all sleeping out on an open veranda and this in winter at an elevation of 2000 feet. Serving under him at Parramatta, I observed his capacity as an organizer—as superintendent and as inspector-general, on his taking up new duties, he at once instituted a searching survey, and this embodied every feature of hospital life. His exhaustive clinical notes remain as his witness of thoroughness and his care and solicitude for his staff procured him wonderful service.

CLARENCE READ.

WE regret to announce the death of Dr. Clarence Read, which occurred on May 24, 1951, at Chatswood, New South Wales.

Medical Practice.

POLICE OFFENCES (AMENDMENT) ACT, 1908, AS AMENDED.

THE following proclamation appeared in the *Government Gazette* of the State of New South Wales, Number 83, of May 18, 1951.

I, Sir John Northcott, Knight Commander of the Most Distinguished Order of Saint Michael and St. George, Companion of the Most Honourable Order of the Bath, Member of the Royal Victorian Order, Lieutenant-General on the Retired List of the Australian Military Forces, Governor of the State of New South Wales and its Dependencies, in the Commonwealth of Australia, with the advice of the Executive Council, do, by this my Proclamation, declare that Part VI of the Police Offences (Amendment) Act, 1908, as amended, shall apply to:

Amidone (also known as Methadon and Dolophine) (6-Dimethylamino-4: 4-diphenylheptan-3-one), its salts and any preparation, admixture, extract or other substance containing not less than one-fifth per centum of amidone.

Pethidine (also known as Dolantin and Demerol) (Ethyl-4-phenyl-1-methylpiperidine-4-carboxylate), its salts and any preparation, admixture, extract or other substance containing not less than one-fifth per centum of pethidine.

Alphaprodine (α-4-Propionoxy-4-phenyl-1: 3-dimethyl-4-piperidine), its salts and any preparation, admixture, extract or other substance containing not less than one-fifth per centum of alphaprodine.

Betaprodine (β-4-Propionoxy-4-phenyl-1: 3-dimethyl-4 piperidine), its salts and any preparation, admixture, extract or other substance containing not less than one-fifth per centum of betaprodine.

Hydroxypethidine (Ethyl 4-*m*-hydroxyphenyl-1-methyl-piperidine-4-carboxylate), its salts and any preparation, admixture, extract or other substance containing not less than one-fifth per centum of hydroxypethidine.

Isoamidone (6-Dimethylamino-4: 4-diphenyl-5-methyl-hexan-3-one), its salts and any preparation, admixture, extract or other substance containing not less than one-fifth per centum of isoamidone.

Ketobemidone (4-Propionyl-4-*m*-hydroxyphenyl-1-methyl-piperidine), its salts and any preparation, admixture, extract or other substance containing not less than one-fifth per centum of ketobemidone.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MAY 5, 1951.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Ankylostomiasis	*	..	..	..	..	..	..	..	..
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	2	2	1(1)	..	..	..	..	..	5
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	2	..	3(3)	..	..	..	5
Diphtheria	9(3)	1(1)	4(2)	..	11(5)	..	..	..	25
Dysentery (Amœbic)	*	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	*	1(1)	2(2)	..	..	..	..	..	3
Encephalitis Lethargica	1	..	2	..	..	..	..	..	3
Erysipelas	*	*	*	2(2)	*	*	..	..	2
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	..	*	*	..	*	*	..	..
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	..	..	*	*	*	*	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	*	..	3(3)	..	..	..	..	..	3
Measles	*	*	*	32(3)	*	*	..	1	33
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	44(21)	8(2)	33(7)	22(17)	1(1)	1	..	..	109
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	5(4)	..	..	..	..	..	5
Rubella(*c*)	*	*	..	*	1	*	..	..	1
Scarlet Fever	24(9)	25(16)	1	4(3)	3(2)	1	..	..	58
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	..	*	1(1)	*	*	*	1
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(*d*)	22(15)	38(23)	12(4)	10(10)	6(6)	4(4)	..	..	92
Typhoid Fever(*e*)	..	..	..	..	1	..	..	..	1
Typhus (Endemic)(*f*)	1(1)	..	2	..	2(2)	..	..	..	5
Undulant Fever	..	1	..	..	..	..	..	..	1
Weil's Disease(*g*)	*	*	1	*	*	*	*	*	1
Whooping Cough	*	*	*	6(3)	*	*	..	..	6
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from the Northern Territory.
* Not notifiable.
(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Methadol (6-Dimethylamino-4: 4-diphenylheptan-3-ol), its salts and any preparation, admixture, extract or other substance containing not less than one-fifth per centum of methadol.

Methadyl acetate (6-Dimethylamino-4: 4-diphenyl-3-heptyl acetate), its salts and any preparation, admixture, extract or other substance containing not less than one-fifth per centum of methadyl acetate.

Phenadoxone (also known as Heptalgin) (6-Morpholino-4: 4-diphenylheptan-3-one), its salts and any preparation, admixture, extract or other substance containing not less than one-fifth per centum of phenadoxone;

in the same manner as it applies to the drugs mentioned in paragraph (a) of subsection 2 of section 18 of the said Act.

The following Proclamations and part of Proclamation are hereby repealed:

(a) Proclamation published in Government Gazette No. 21 of 27th February, 1948, relating to Pethidine.

(b) That part of Proclamation published in Government Gazette No. 94 of 13th August, 1948, relating to Amidone.

(c) Proclamation published in Government Gazette No. 190 of 15th December, 1950, relating to Alphaprodine, Betaprodine, Hydroxypethidine, Isoamidone, Ketobemidone, Methadol, Methadyl Acetate and Phenadoxone.

Signed and sealed at Sydney, this second day of May, one thousand nine hundred and fifty-one.

By His Excellency's Command,

CLIVE EVATT.

Advice has been received from the Under Secretary to the New South Wales Chief Secretary's Department that the withdrawal of the authority of Mr. Lawrence Leong as a pharmacist under the *Police Offences (Amendment) Act*, to have in his possession and to retail, compound and dispense drugs to which the Act applies, ceased to operate on and from May 18, 1951.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Week-End Course at Broken Hill.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that, in conjunction with the Broken Hill Medical Association, a week-end course will be held at the Broken Hill and District Hospital on Saturday and Sunday, June 9 and 10, 1951. The programme is as follows:

Saturday, June 9: 2.30 p.m., "Coronary Disease and Cardiac Pain", Dr. John Halliday; 4 p.m., "The Painful Shoulder", Dr. Norman Little.

Sunday, June 10: 10 a.m., "Non-Hæmorrhagic Vaginal Discharge", Dr. Clement Chapman; 11.30 a.m., "Some Aspects of Congenital Heart Disease", Dr. John Halliday; 2.30 p.m., "Internal Derangement of the Knee", Dr. Norman Little; 4 p.m., "The Choice of Surgical Procedure in Uterine Prolapse", Dr. Clement Chapman.

The fee for attendance will be £2 2s. Those wishing to attend are requested to communicate with Dr. J. T. Cullen, Honorary Secretary, Broken Hill Medical Association, Broken Hill, New South Wales, as soon as possible.

Clinical Meeting at Balmoral Naval Hospital.

A clinical meeting will be held at the Balmoral Naval Hospital, Balmoral, Sydney, on Tuesday, June 19, 1951, at 2 p.m., when Dr. J. Kempson Maddox will speak on "Recent Advances in Cardiology". Clinical cases will be shown at 4 p.m., after afternoon tea, and all members of the medical profession are invited to attend.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Ackary, John Francis, M.B., B.S., 1951 (Univ. Sydney), St. George Hospital, Kogarah.

McKenzie, Nancy, M.B., B.S., 1951 (Univ. Sydney), Broken Hill and District Hospital, Broken Hill.

Gerdes, William Thomas, M.B., B.S., 1945 (Univ. Sydney), 7 Moore Street, Austinmer.

Reid, Stanley Edward, M.B., B.S., 1950 (Univ. Melbourne), Manly District Hospital, Manly.

Halloran, Audrey, M.B., B.S., 1951 (Univ. Sydney), St. George Hospital, Kogarah.

Diary for the Month.

JUNE 5.—New South Wales Branch, B.M.A.: Organization and Science Committee.
JUNE 6.—Victorian Branch, B.M.A.: Branch Meeting.
JUNE 6.—Western Australian Branch, B.M.A.: Council Meeting.
JUNE 7.—South Australian Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £4 *per annum* within Australia and the British Commonwealth of Nations, and £5 *per annum* within America and foreign countries, payable in advance.